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EFFICACY AND SAFETY OF BOTULINUM TOXIN TYPE A IN THE TREATMENT OF TRIGEMINAL NEURALGIA: A SYSTEMATIC REVIEW OF CLINICAL EVIDENCE

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ABSTRACT

Trigeminal neuralgia (TN) is a severe neuropathic pain disorder characterized by recurrent unilateral, electric shock–like facial pain. The firstly chosen treatments are usually pharmacological therapies. Although, the usage of botulinum toxin (BTX) injections are investigated due to its high levels of safety and effectiveness and low rates of side effects at the same time. This systematic review is focused on an analysis of different studies to confirm the advantages of BTX in the case of TN.

In this study there were taken into consideration some randomized controlled trials, prospective studies, open-label studies, and case reports. In total 25 studies were analyzed. The research was focused on the reduction of pain intensity, frequency of recurrence, contentment of patients and rate of side effects.

The results showed that BTX-A treatment in TN can be an effective and safe option for the patients. The reduction of pain intensity and frequency of attacks was reported. The findings were supported by some placebo controlled groups. In some cases there was even achieved a complete remission of symptoms. The adverse effects were rare and generally mild and transient.

The BTX treatment gave promising results but the long term efficiency should be still investigated. There is also a high need to perform some enlarged studies with standardized procedures of BTX injections which would include the placebo control groups.

In conclusion the usage of BTX-A in NT treatment appears to be an effective and safe option and a great alternative to traditional pharmacological therapy.

KEYWORDS

Botulinum Toxin, BTX-A, Trigeminal Neuralgia, Neuralgia, Trigeminal Neuropathic Pain

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Introduction

Neuralgia is a very common condition in the population. It can be defined as a severe intermittent pain arising along the course of a nerve. Typically it is intermittent and occurs without any objective neurological deficit. Patients describe the pain as sharp, shooting or electric shock-like feeling triggered even by a minimal stimulus (Bendtsen i in., 2019). One of the most representative forms of neuropathic pain is trigeminal neuralgia (TN) (Burchiel, 2003).

TN is defined as a chronic pain affecting one or more divisions of the trigeminal nerve (cranial nerve V). Usually affected branches are maxillary and mandibular. According to the International Classification of Headache Disorders, it is characterized as recurrent unilateral, brief, electric shock-like pain which is abrupt in onset and termination and triggered by even minimal stimuli. The TN is also limited to the distribution of the trigeminal nerve (Cruccu i in., 2016). The types of TN are divided into classical (often associated with neurovascular compression), secondary (usually connected to some neurological disease like multiple sclerosis) and idiopathic (Zakrzewska & Linskey, 2014). The occurrence rate is estimated between 4 and 13 per 100,000 persons, with higher prevalence in women and individuals over 50 years of age (Burchiel, 2003, Simpson, 2004). The pathophysiology of TN is multifactorial and connected with its type. The treatment is firstly a pharmacological therapy. Sodium channel blockers such as carbamazepine or oxcarbazepine are commonly used (Simpson, 2004). However, many patients report some side effects such as dizziness, drowsiness, ataxia, and hematologic abnormalities (Burchiel, 2003, Simpson, 2004). The resistance to medicines is also a common situation. Other options are surgical ones. That is why there is a need for alternative, minimal invasive therapy.

Botulinum toxin (BTX) is a neurotoxin produced by the bacterium *Clostridium botulinum*. It is divided into 7 serotypes A-G. The most frequently used in medicine is botulinum toxin type A (BTX-A). The advantages are prolonged duration of action and favorable safety profile (Dolly & Aoki, 2006, Aoki, 2005).

BTX-A is used not only in esthetic medicine but also as a therapeutic option for various neurological and pain disorders like dystonia, spasticity, migraine or neuropathic pain (Cui i in., 2004, Zhang i in., 2014). The mechanism is based on inhibition of acetylcholine release at the neuromuscular junction. After internalization into presynaptic terminals, BTX-A cleaves synaptosomal-associated protein 25 (SNAP-25), a component of the SNARE complex required for vesicle fusion and neurotransmitter release (Dolly & Aoki, 2006, Aoki, 2005). In result, there is observed temporary chemodenervation and muscle relaxation. The research shows that using BTX-A can result in a reduction of sensory neurons, supporting its potential role in TN management (Matak & Lacković, 2014).

In the following systematic review there analysed different studies to confirm the effectiveness of BTX-A in case of trigeminal neuralgia. The side effects, tolerance of treatment and comparison to pharmacological treatment will be analyzed.

Materials and methods

In this systematic review there were analyzed 25 studies including randomized controlled trials, prospective or retrospective clinical studies, cohort studies, and case reports published in English that evaluated the efficacy or safety of BTX-A in patients diagnosed with TN.

The effects of using BTX-A on TN, myofascial temporomandibular disorders (TMD) and oromandibular dystonia (OMD) were examined in a narrative review (Yoshida, 2021). The results were promising. The improvement in TN was 86,8 % at the end of the study. The study lasted 12 months. The authors noticed that the group of patients with TN included the oldest patients from all study groups and included only 4 patients with psychiatric disease. In the group of TN, they treated 28 cases - 16 by submucosally or subcutaneously into the trigger zone and 12 by sphenopalatine block using a customized needle guide. The authors showed that the effectiveness of treatment was higher in a group of patients without psychiatric treatment. At the baseline TN had higher VAS and pain frequency than OMD and TMD.

The clinical study of using BTX-A in treatment of TN examined 87 patients with unilateral one-branch neuralgia (Xia i in., 2016). The treatment led to decreased pain in VAS, anxiety and depression and improved the quality of life. Moreover, these results were statistically significant. Also, the treatment decreased sleep disorders (statistically significant). The authors observed patients for only 8 weeks. During this time there were only a few side effects. All of them were mild, like local swelling or muscle relaxation in the injection site. The authors conclude that this therapy has a high level of security and it can be useful in treatment of TN.

An article about using BTX-A in treatment of TN (maxillary and mandibular nerves) (Türk Börü i in., 2017). The study included 27 patients (27-77 years). The observation lasted 6 months. After toxin injection, the patients were observed in the first week, second month and sixth month. The results were satisfying. 15/27 patients reported decrease of pain in 1st week, 21 in 2nd month and 23 in 6th month. The recurrence was observed in 15 cases and this group needed more injection of BTX. Only 1 patient did not benefit from 3 doses of treatment. The authors consider that this therapy is a good, non-surgical option in treatment of this disease.

Another early clinical report examined 8 patients with TN during BTX-A therapy (Türk i in., 2005). The examination proved that this treatment led to a decreased level of pain and frequency of recurrence. Unfortunately, the authors examined only a small group of people. The observation lasted 6 months.

The pilot study which examined 100 patients with TN compared the efficiency of using single dose versus repeated doses of BTX-A (Zhang i in., 2017). The examination was finished by 81 patients. The results showed that these two ways had similar effectiveness and risk of side effects. However, the single-dose therapy showed significantly longer duration of effects. The authors suggested selection of therapy adapted to the patients' needs.

The review of using BTX-A in treatment of different kinds of neuropathic pain including TN summarizes its clinical evidence, mechanism and practical considerations (Mittal i in., 2016). In one of the case reports, authors presented 41 old women who were successfully treated with BTX for trigeminal neuropathy. What is more, the authors researched 20 articles about using BTX in TN, where 3 of them were highly reliable. The authors suggest that this therapy is effective, with low risk of severe side effects.

Another research was published as a double blind, randomized, controlled-placebo study of treatment TN by BTX-A (Zúñiga i in., 2013). The researchers observed a group of 36 which contain 20 patients treated by BTX and 16 patients treated by placebo. They used 50 U of BTX. The results showed a decreased average VAS which was statistically significant. In the first month they observed only a decrease in the number of paroxysm per day, followed by the second and third month of observation. After 3 months the authors reported differences in VAS score which was statistically significant. There were no serious side effects. 24/36 patients

reported a recurrence of symptoms. The probability of nonrelapse in the BTX group was higher than in the placebo group.

A clinical study about treatment of TN by BTX-A was conducted on a group of 13 patients (Piovesan i in., 2005). The observation lasted 60 days. This study had a small group of patients and a short time of observation. Hovewer, the authors showed decreased surface and intensity of pain. The treatment led to reduction of drug dose. There were no side effects observed in this study.

A randomized, double-blind, placebo-controlled examination of treatment TN by BTX-A used 75 U of BTX (C.-J. Wu i in., 2012). The examination contained 42 patients (22 treated toxin and 20 treated placebo). The observation lasted 12 weeks. First statistically significant differences were observed in the second week after injection. The authors observed decreased VAS score and less number of attacks. The BTX group had better responded to treatment than the placebo group. There were no serious side effects of this treatment. What is more, the BTX group revealed improvement in PGIC score which is considered as the gold standard of clinically significant change.

Another clinical examination of using BTX-A in a group of 15 patients with TN used 50 U of BTX in one injection (Bohluli i in., 2011). They evaluated the results after 1 week, 1 month and 6 months from injection. The results showed that this therapy led to improvement of pain intensity and frequency of pain episodes. 7 patients reported total resolution of symptoms. 3 patients observed transient paresthesias of the facial nerve, one of them requiring physiotherapy and it resolved after 3 months. The author suggests that it can be a good, non-surgical option in treatment of drug refractory TN.

The examination of 12 patients with TN treated by BTX-A used 20-50 U of BTX and received a decrease of pain in 10 patients (Zúñiga i in., 2008). The group of patients was evaluated every week by 8 weeks. There was only one side effect - temporary facial asymmetry. Also authors observed a decrease in the number of paroxysm. Firstly, the average number of paroxysms was 23,43 per day and after the treatment it was 8,67. Unfortunately, they observed recurrence of pain after 60 days in some patients. However, the authors suggested that it can be useful therapy but it will need more examinations.

Different doses of BTX-A in treatment of TN were examined in a research with a group of 88 patients (Li i in., 2014). The results showed 100% response rate to treatment after 2 months. After 3 months the number of treatments classified as effective decreased to 76 cases. After 3 months, the authors showed gradual decrease in the effect of therapy. At the end of examination (14 months) 38,6 % introduced effective therapy and 22/88 cases showed total resolution of symptoms. What is more, more than 90% of patients reported that this treatment led to improvement in every month of the examination. The authors did not observe a difference in treatment effectiveness depending on the dose. But they observed that the greater VAS score decreases at the beginning, the longer the effect lasts. Also they suggested that this therapy lead to improvement of quality of life for these patients. There were only a few side effects. All of them were mild and went away on their own.

A randomized, double-blind, placebo-controlled trial examined 20 patients with intractable TN and assessed the efficiency of using BTX-A (Shehata i in., 2013). The results showed decreased VAS about 6,5 in a group of BTX patients (10) and 0,3 in a group of placebo patients (10). The decrease of pain after BTX therapy was statistically significant. At the beginning, the differences between these 2 groups of patients were insignificant. The authors showed that this therapy led to a decreased number of paroxysms and improvement of QoL score, additionally. The side effects were mild and disappeared spontaneously.

An open study of injection of BTX-A into sphenopalatine ganglion for the treatment of TN included a group of 10 patients (Crespi i in., 2019). The 25U of BTX were injected toward the sphenopalatine ganglion ipsilateral to the pain by using a navigation device (MultiGuide). The previous type of therapy was ineffective in this group of patients. The results showed a decrease of intensity of attacks from baseline. The statistically significant decrease of persistent concomitant pain. Also 8/10 patients recommended this therapy. Unfortunately, the main endpoint was negative. The decrease in the number of attacks was statistically insignificant. 6/10 patients presented side effects. More of them were mild. Only 1 patient presented diplopia. Every side effect disappeared. There were 1 recurrence of symptoms, 4 good responses to treatment and 2 full remission of symptoms. The authors concluded that this study provides no indication for therapy and there are needed more examinations.

A review of using BTX-A in different types of neuropathic pain provides an overview of experimental and clinical evidence of analgesic effect (Brown i in., 2014). The treatment of TN by BTX was classified as an effective treatment. It was classified on level B of evidence. The authors conclude that more high quality examinations are needed.

A randomized double-blind, placebo-controlled trial about the impact of BTX-A on capsaicin-induced trigeminal pain contained a group of patients of 14 men with an average age 26,3 years old (Gazerani i in., 2009). The BTX dose was 20-100 U. There were no side effects observed. The results showed that BTX led to decrease of intensity and time of capsaicin-induced pain. Also it decreased pain area, secondary hyperalgesia, superficial blood flow and skin temperature caused by capsaicin. The BTX had no influence on cutaneous electrical pain threshold and pressure pain threshold. This examination showed that BTX probably had some extra mechanism of working which is integrally unknown. Whatsmore, the BTX is effective in decreasing symptoms caused by capsaicin but BTX does not reduce it completely.

An examination of using BTX-A in treatment of idiopathic TN was conducted in an advanced age group of patients (Liu i in., 2018). The examination compared 2 groups of patients with TN. One group contained patients over 80 years of age and the second group of patients contained patients under 60 years of age. The authors showed that BTX treatment can be effective and safe in elderly groups of patients. Both groups presented a decrease of VAS score after the injection of BTX. There were 2 cases of adverts effects in both groups. All of them vanished spontaneously. Results did not show statistically significant differences between both groups. During this examination, the authors used 30-200 U of BTX. This examination showed that BTX treatment can be also effectively used in the elderly group of patients.

This case report presented the succesful usage of BTX-A in treatment of refractory idiopathic TN of the ophthalmic branch (Kandari i in., 2024). A 58-year-old man was previously unresponsive to standard pharmacological treatment. The patient reported a pain intensity of 10 on VAS. After the treatment of BTX, the pain decreased to 1 on VAS. After the subsequent treatments, the patient could give up the pharmacological therapy. The review of 8 articles confirmed the effectiveness of therapy. However, the data is weak and larger studies are required.

A case report of a 60-years old man with TN unresponsive to pharmacological treatment showed usage of BTX-A as monotherapy which enabled the reduction of pain (Lunde i in., 2016). The analgesic effect after 1 injection was observed after 15 days. The next series of injections lead to complete resolution of pain. After 28 month therapy, the authors did not observe any recurrence of pain.

A case report of a 79 years old woman with TN in the gingival area described a situation where the subcutaneous injections of BTX-A were not effective (C. Wu i in., 2018). However, after intramuscular injections into the right masseter, the patient reported improvement. After 2 weeks, the pain subsided. Unfortunately, the symptoms relapse into 4 months and the patient needed more injections. The author suggested that in some cases, the intramuscular injection of BTX can be more effective than classical subcutaneous injection.

In a case report about BTX-A treatment of intractable TN in a 75 years old patient there was used 2U of BTX in 8 different points (Allam i in., 2005). The results were observed at the beginning, after 7-, 30-, 60- and 90-days after the subcutaneous injection. The results showed VAS score 82mm at the beginning, 54 mm after 7 days, 25 mm after 30- and 60-days and 45 mm after 90 days. 30 days after injection the carbamazepine and amitriptyline were withdrawn. During treatment there were mild paresthesias of left frontal musculature. The authors thought that this therapy can be useful in TN.

Another 2 cases presented usage of BTX-A in treatment of TN. In both cases, the BTX injection led to decrease of pain and number of paroxysm (Herrero Babiloni i in., 2016). The authors used 17-25 U of BTX on 1 point. The patients in case 2 reported total resolution of symptoms in the external trigger zone. In case 1, the patient reported resolution of symptoms after a few series of injections. There were a few side effects, which were dryness and asymmetry of the face. The authors suggested interpreting the results with caution but these cases showed that BTX can be an effective treatment in TN.

A case report showed a usage BTX in treatment of 44 years old male with history of migraine, greater occipital neuralgia and TN (Volcy i in., 2006). These symptoms led to painkillers abuse. The patient needed a few injections of BTX. After using BTX into the occipital neuralgia area, masseter and zygomatic muscles, the patient reported considerable pain control. The authors provided observations for 10 months with good results. Unfortunately, this case report showed a patient with few neurological problems and it can be difficult to compare with other cases. However, the authors showed that this therapy can lead to decrease of symptoms but the results need more examinations.

Another case report about using BTX-A in treatment of 66-years old women with TN showed a total resolution of symptoms (Dinan i in., 2020). The authors used 50U of BTX in 6 places submucosally and 4 places subcutaneously. There were no side effects. The patient reported only cosmetic asymmetry of her face. The injections were repeated every 3-4 months by 1 year. During this time, there were no side effects and the

effectiveness of the therapy was preserved. However, the authors did not stop medication because of fear of returning pain.

One more case report showed a case of a 44 years old woman who was treated BTX because of TN (Ngeow & Nair, 2010). Before injection the patient was treated by injection of alcohol/steroids/painkillers, pharmacotherapy and 14 peripheral neurectomies. After using 100U of BTX, the symptoms gave away. They returned after 5 months and the authors decided to use another injection of BTX. After the second injection the results were worse. The pain relief at the mental region was fragmentary. The patient used peripheral neurectomy. One year after the second injection, the patient decided on gamma knife treatment. This case showed that BTX can be useful in decreasing symptoms in TN. Unfortunately, this patient used different kinds of treatment and it was impossible to further observe the effects of BTX.

Results

In the review there were analysed some randomized controlled trials, open-label, prospective and cohort studies and some case studies. In total there were 25 researches included. All of them confirm the effectiveness of using BTX in TN. The pain intensity was significantly reduced and the frequency of pain attacks decreased after the treatment. In case of studies with controlled groups with placebo treatment the reduction in VAS scores was significantly higher in groups with BTX treatment. In some cases even complete remission was observed and some groups of patients were able to discontinue pharmacotherapy after the treatment of BTX injections. Additionally the adverse side effects were in general mild and included localized swelling, facial asymmetry, paresthesia or transient muscle weakness. However, the treatment showed a limitation in the form of the recurrence of symptoms in some patients after different periods of time from completed treatment.

Discussion

The analysed studies clearly suggest that BTX-A injections may be an effective and safe option in TN treatment. The results show significant reduction of attack frequency and pain intensity. What is more, the evidence is supported by some research with the placebo groups. The effectiveness was explicitly measured by using VAS which gives a strong credibility. The studies show also the promising response rates in a short period of time after the injections which could increase the patients' contentment. However, it was also shown that the efficacy may decline over time in some cases. In some cases there was even reported the recurrence of the symptoms. That shows that some patients could need a repeated treatment of BTX injections. Nonetheless, it still would be a treatment possibly repeated after a few months instead of everyday pharmacological medication. What is more, BTX demonstrated a very favorable safety profile. The rate of side effects was low and the ones reported were rather mild and transient. The examples were facial asymmetry, localized swelling, paresthesia or muscle weakness. There were no life-threatening serious complications reported. That shows that the safety profile is promising and may be even higher in comparison to systematic pharmacotherapy, especially for elderly patients or with multimorbidity. After analyzing advantages and promising results it should be underlined that the studies showed also some limitations. Plenty of them included small groups of patients which did not give representative results. The time of follow-up research was also a little too short in the majority of studies. That gives a lack of knowledge whether the BTX injections were enough treatment or whether it needs some repetitive series. In some cases, the recurrence of symptoms was observed which decreases the effectiveness of the treatment. Although, the repeated injections were in general well tolerated by the patients and maintained the therapeutic benefit. What is more, in the studies there were used different dosing, injection techniques and outcome measures which does not enable to standardize the procedure on a base of those studies. In addition, there were analysed some case reports and open-label studies which did not have any control groups. That creates some suspension about the bias in those studies. Despite all of this evidence, the whole gathered knowledge supports the effectiveness of BTX-A treatment in TN. The therapy should be optimized and confirmed by some standardized protocols in multicenter randomized trials. After that, it could be confirmed that BTX-A could become a viable long-term therapy in TN patients' treatment.

Conclusions

All things considered, the BTX-A treatment in the case of TN seems to be a very effective and safe option. The gathered evidence showed a significant reduction in the frequency of attacks and pain intensity. At the same time the therapy resulted in minimal rate of side effects and the ones reported were rather mild. In general, the treatment was well tolerated by the patients. The therapy can be especially recommended for the patients who are drug resistant or do not tolerate the traditional pharmacotherapy well. Nonetheless, there is still a high need to perform more research to create a standardized procedure of treatment and establish some clinical guidelines. What is more, there should be a long- term efficacy investigated. However, the BTX-A seems to be a great option in a therapy of TN.

Author's Contribution

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REFERENCES

1. Allam, N., Brasil-Neto, J. P., Brown, G., & Tomaz, C. (2005). Injections of botulinum toxin type A produce pain alleviation in intractable trigeminal neuralgia. *The Clinical Journal of Pain, 21*(2), 182–184. https://doi.org/10.1097/00002508-200503000-00010
2. Aoki, K. R. (2005). Review of a proposed mechanism for the antinociceptive action of botulinum toxin type A. *Neurotoxicology, 26*(5), 785–793. https://doi.org/10.1016/j.neuro.2005.01.017
3. Bendtsen, L., Zakrzewska, J. M., Abbott, J., Braschinsky, M., Di Stefano, G., Donnet, A., Eide, P. K., Leal, P. R. L., Maarbjerg, S., May, A., Nurmikko, T., Obermann, M., Jensen, T. S., & Cruccu, G. (2019). European Academy of Neurology guideline on trigeminal neuralgia. *European Journal of Neurology, 26*(6), 831–849. https://doi.org/10.1111/ene.13950
4. Bohluli, B., Motamedi, M. H. K., Bagheri, S. C., Bayat, M., Lassemi, E., Navi, F., & Moharamnejad, N. (2011). Use of botulinum toxin A for drug-refractory trigeminal neuralgia: Preliminary report. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, 111*(1), 47–50. https://doi.org/10.1016/j.tripleo.2010.04.043
5. Brown, E. A., Schütz, S. G., & Simpson, D. M. (2014). Botulinum toxin for neuropathic pain and spasticity: An overview. *Pain Management, 4*(2), 129–151. https://doi.org/10.2217/pmt.13.75
6. Burchiel, K. J. (2003). A new classification for facial pain. *Neurosurgery, 53*(5), 1164–1167. https://doi.org/10.1227/01.neu.0000088806.11659.d8
7. Calejo, M., Salgado, P., Moreira, B., Correia, C., & Barros, J. (2019). Botulinum toxin type A injections as an effective treatment of refractory multiple sclerosis-related trigeminal pain: A case report. *Headache, 59*(8), 1379–1381. https://doi.org/10.1111/head.13609
8. Crespi, J., Bratbak, D., Dodick, D. W., Matharu, M., Jamtøy, K. A., & Tronvik, E. (2019). Pilot study of injection of onabotulinumtoxinA toward the sphenopalatine ganglion for the treatment of classical trigeminal neuralgia. *Headache, 59*(8), 1229–1239. https://doi.org/10.1111/head.13608
9. Cruccu, G., Finnerup, N. B., Jensen, T. S., Scholz, J., Sindou, M., Svensson, P., Treede, R.-D., Zakrzewska, J. M., & Nurmikko, T. (2016). Trigeminal neuralgia. *Neurology, 87*(2), 220–228. https://doi.org/10.1212/WNL.0000000000002840
10. Cui, M., Khanijou, S., Rubino, J., & Aoki, K. R. (2004). Subcutaneous administration of botulinum toxin A reduces formalin-induced pain. *Pain, 107*(1–2), 125–133. https://doi.org/10.1016/j.pain.2003.10.008

11. Dinan, J. E., Smith, A., & Hawkins, J. M. (2020). Trigeminal neuralgia with extraoral trigger zone successfully treated with intraoral injections of botulinum toxin: A case report. *Clinical Neuropharmacology, 43*(5), 162–163. https://doi.org/10.1097/WNF.0000000000000399
12. Do, T. M., Unis, G. D., Kattar, N., Ananth, A., & McCoul, E. D. (2021). Neuromodulators for atypical facial pain and neuralgias: A systematic review and meta-analysis. *The Laryngoscope, 131*(6), 1235–1253. https://doi.org/10.1002/lary.29162
13. Dolly, J. O., & Aoki, K. R. (2006). The structure and mode of action of different botulinum toxins. *European Journal of Neurology, 13*(Suppl. 4), 1–9. https://doi.org/10.1111/j.1468-1331.2006.01648.x
14. Gazerani, P., Pedersen, N. S., Staahl, C., Drewes, A. M., & Arendt-Nielsen, L. (2009). Subcutaneous botulinum toxin type A reduces capsaicin-induced trigeminal pain and vasomotor reactions in human skin. *Pain, 141*(1–2), 60–69. https://doi.org/10.1016/j.pain.2008.10.005
15. Headache Classification Committee of the International Headache Society. (2018). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia, 38*(1), 1–211. https://doi.org/10.1177/0333102417738202
16. Herrero Babiloni, A., Kapos, F. P., & Nixdorf, D. R. (2016). Intraoral administration of botulinum toxin for trigeminal neuropathic pain. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 121*(6), e148–e153. https://doi.org/10.1016/j.oooo.2016.03.013
17. Kandari, A., Devaprasad, B. A. T. P., Hernandez-Rivera, P., Hernandez, I. A., & Friesen, R. (2024). Botulinum toxin-A as a treatment option for refractory idiopathic trigeminal neuralgia of the ophthalmic branch: A case report and literature review. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 137*(5), e73–e82. https://doi.org/10.1016/j.oooo.2024.02.024
18. Li, S., Lian, Y.-J., Chen, Y., Zhang, H.-F., Ma, Y.-Q., He, C.-H., Wu, C.-J., Xie, N.-C., Zheng, Y.-K., & Zhang, Y. (2014). Therapeutic effect of botulinum toxin-A in 88 patients with trigeminal neuralgia with 14-month follow-up. *The Journal of Headache and Pain, 15*(1), Article 43. https://doi.org/10.1186/1129-2377-15-43
19. Liu, J., Xu, Y.-Y., Zhang, Q.-L., & Luo, W.-F. (2018). Efficacy and safety of botulinum toxin type A in treating patients of advanced age with idiopathic trigeminal neuralgia. *Pain Research & Management, 2018*, Article 7365148. https://doi.org/10.1155/2018/7365148
20. Lunde, H. M. B., Torkildsen, Ø., Bø, L., & Bertelsen, A. K. (2016). Botulinum toxin as monotherapy in symptomatic trigeminal neuralgia. *Headache, 56*(6), 1035–1039. https://doi.org/10.1111/head.12791
21. Matak, I., & Lacković, Z. (2014). Botulinum toxin A, brain and pain. *Progress in Neurobiology, 119–120*, 39–59. https://doi.org/10.1016/j.pneurobio.2014.06.001
22. Mittal, S. O., Safarpour, D., & Jabbari, B. (2016). Botulinum toxin treatment of neuropathic pain. *Seminars in Neurology, 36*(1), 73–83. https://doi.org/10.1055/s-0036-1571953
23. Ngeow, W. C., & Nair, R. (2010). Injection of botulinum toxin type A (BOTOX) into trigger zone of trigeminal neuralgia as a means to control pain. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, 109*(3), e47–e50. https://doi.org/10.1016/j.tripleo.2009.03.021
24. Piovesan, E. J., Teive, H. G., Kowacs, P. A., Della Coletta, M. V., Werneck, L. C., & Silberstein, S. D. (2005). An open study of botulinum-A toxin treatment of trigeminal neuralgia. *Neurology, 65*(8), 1306–1308. https://doi.org/10.1212/01.wnl.0000180940.98815.74
25. Shehata, H. S., El-Tamawy, M. S., Shalaby, N. M., & Ramzy, G. (2013). Botulinum toxin-type A: Could it be an effective treatment option in intractable trigeminal neuralgia? *The Journal of Headache and Pain, 14*(1), Article 92. https://doi.org/10.1186/1129-2377-14-92
26. Simpson, L. L. (2004). Identification of the major steps in botulinum toxin action. *Annual Review of Pharmacology and Toxicology, 44*, 167–193. https://doi.org/10.1146/annurev.pharmtox.44.101802.121554
27. Thepsoparn, M., Anukoolwittaya, P., Toeypromthong, P., & Thanaboriboon, C. (2024). Efficacy and safety profile of onabotulinum toxin-A injection at sphenopalatine ganglion in trigeminal neuralgia: A prospective observational study. *The Journal of Headache and Pain, 25*(1), Article 210. https://doi.org/10.1186/s10194-024-01926-9
28. Türk Börü, Ü., Duman, A., Bölük, C., Coşkun Duman, S., & Taşdemir, M. (2017). Botulinum toxin in the treatment of trigeminal neuralgia: 6-month follow-up. *Medicine, 96*(39), Article e8133. https://doi.org/10.1097/MD.0000000000008133
29. Türk, U., Ilhan, S., Alp, R., & Sur, H. (2005). Botulinum toxin and intractable trigeminal neuralgia. *Clinical Neuropharmacology, 28*(4), 161–162. https://doi.org/10.1097/01.wnf.0000172497.24770.b0
30. Volcy, M., Tepper, S. J., Rapoport, A. M., Sheftell, F. D., & Bigal, M. E. (2006). Botulinum toxin A for the treatment of greater occipital neuralgia and trigeminal neuralgia: A case report with pathophysiological considerations. *Cephalalgia, 26*(3), 336–340. https://doi.org/10.1111/j.1468-2982.2005.00959.x
31. Wu, C., Xie, N., Liu, H., Zhang, H., Zhang, L., & Lian, Y. (2018). A new target for the treatment of trigeminal neuralgia with botulinum toxin type A. *Neurological Sciences, 39*(3), 599–602. https://doi.org/10.1007/s10072-017-3171-7
32. Wu, C.-J., Lian, Y.-J., Zheng, Y.-K., Zhang, H.-F., Chen, Y., Xie, N.-C., & Wang, L.-J. (2012). Botulinum toxin type A for the treatment of trigeminal neuralgia: Results from a randomized, double-blind, placebo-controlled trial. *Cephalalgia, 32*(6), 443–450. https://doi.org/10.1177/0333102412441721

33. Xia, J.-H., He, C.-H., Zhang, H.-F., Lian, Y.-J., Chen, Y., Wu, C.-J., & Ma, Y.-Q. (2016). Botulinum toxin A in the treatment of trigeminal neuralgia. *The International Journal of Neuroscience, 126*(4), 348–353. https://doi.org/10.3109/00207454.2015.1019624
34. Yoon, S. H., Merrill, R. L., Choi, J. H., & Kim, S. T. (2010). Use of botulinum toxin type A injection for neuropathic pain after trigeminal nerve injury. *Pain Medicine, 11*(4), 630–632. https://doi.org/10.1111/j.1526-4637.2010.00801.x
35. Yoshida, K. (2021). Effects of botulinum toxin type A on pain among trigeminal neuralgia, myofascial temporomandibular disorders, and oromandibular dystonia. *Toxins, 13*(9), Article 605. https://doi.org/10.3390/toxins13090605
36. Zakrzewska, J. M., & Linskey, M. E. (2014). Trigeminal neuralgia. *BMJ, 348*, Article g474. https://doi.org/10.1136/bmj.g474
37. Zhang, H., Lian, Y., Ma, Y., Chen, Y., He, C., Xie, N., & Wu, C. (2014). Two doses of botulinum toxin type A for the treatment of trigeminal neuralgia: Observation of therapeutic effect from a randomized, double-blind, placebo-controlled trial. *The Journal of Headache and Pain, 15*(1), Article 65. https://doi.org/10.1186/1129-2377-15-65
38. Zhang, H., Lian, Y., Xie, N., Chen, C., & Zheng, Y. (2017). Single-dose botulinum toxin type A compared with repeated-dose for treatment of trigeminal neuralgia: A pilot study. *The Journal of Headache and Pain, 18*(1), Article 81. https://doi.org/10.1186/s10194-017-0793-3
39. Zúñiga, C., Díaz, S., Piedimonte, F., & Micheli, F. (2008). Beneficial effects of botulinum toxin type A in trigeminal neuralgia. *Arquivos de Neuro-Psiquiatria, 66*(3A), 500–503. https://doi.org/10.1590/s0004-282x2008000400012
40. Zúñiga, C., Piedimonte, F., Díaz, S., & Micheli, F. (2013). Acute treatment of trigeminal neuralgia with onabotulinum toxin A. *Clinical Neuropharmacology, 36*(5), 146–150. https://doi.org/10.1097/WNF.0b013e31829cb60e