

Cancer Association of South Africa (CANSA)



Fact Sheet On the Use of Botox by Cancer Survivors

Introduction

Botox is a drug made from a neurotoxin produced by the bacterium *Clostridium botulinum* called botulinum toxin. It is used medically to treat certain muscular conditions and cosmetically remove wrinkles by temporarily paralyzing muscles.

[Picture Credit: Before and After 1]



Botulinum toxin causes the disease botulism, however it is also used commercially in medicine, cosmetics, and research. There are seven types of botulinum toxin, named type A–G. Type A and B are capable of causing disease in humans, and are also used commercially and medically. Types C–G are less common; types E and F can cause disease in humans, while the other types cause disease in other animals. Botulinum toxin types A and B are used in medicine to treat various muscle spasms and diseases characterised by overactive muscle.

Botulinum toxin is sold commercially under the names:

- Botox, Vistabel, Botox cosmetic (OnabotulinumtoxinA or botulinum toxin type A)
- Dysport (AbobotulinumtoxinA or botulinum toxin type A)
- Bocouture, Xeomin (IncobotulinumtoxinA or botulinum toxin type A)
- Myobloc (RimabotulinumtoxinB or botulinum toxin type B).



BOTOX® Cosmetic is the only FDA-approved treatment to temporarily improve the appearance of both moderate to severe frown lines between the brows and crow's feet in adults.

[Picture Credit: Before and After 2]

In cosmetic applications, botulinum toxin is considered safe and effective for reduction of facial wrinkles, especially in the uppermost third

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of the face. Injection of botulinum toxin into the muscles under facial wrinkles causes relaxation of those muscles, resulting in the smoothing of the overlying skin. Smoothing of wrinkles is usually visible three days after treatment and is maximally visible two weeks following injection. The treated muscles gradually regain function, and generally return to their former appearance three to four months after treatment. Muscles can be treated repeatedly to maintain the smoothed appearance. (Small, 2014).

Indications for the Use of Botox

BOTOX[®] is a prescription medicine that is injected into muscles and used:

- to treat overactive bladder symptoms such as a strong need to urinate with leaking or wetting accidents (urge urinary incontinence), a strong need to urinate right away (urgency), and urinating often (frequency) in adults 18 years and older when another type of medicine (anticholinergic) does not work well enough or cannot be taken
- to treat leakage of urine (incontinence) in adults 18 years and older with overactive bladder due to neurologic disease who still have leakage or cannot tolerate the side effects after trying an anticholinergic medication
- to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years or older
- to treat increased muscle stiffness in elbow, wrist, finger, thumb, ankle, and toe muscles in people 18 years and older with upper and lower limb spasticity
- to treat the abnormal head position and neck pain that happens with cervical dystonia (CD) in people 16 years and older
- to treat certain types of eye muscle problems (strabismus) or abnormal spasm of the eyelids (blepharospasm) in people 12 years and older

BOTOX[®] is also injected into the skin to treat the symptoms of severe underarm sweating (severe primary axillary hyperhidrosis) when medicines used on the skin (topical) do not work well enough in people 18 years and older.

BOTOX[®] Cosmetic is a prescription medicine that is injected into muscles and used to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines) in adults for a short period of time (temporary).

BOTOX[®] Cosmetic is a prescription medicine that is injected into the area around the side of the eyes to improve the look of moderate to severe crow's feet lines in adults for a short period of time (temporary).

Before Going for Botox Treatment

If considering Botox injections, one must be certain about why one wants to have the injections. The injections are expensive, and have their limitations.

Cost - while some practitioners charge a flat rate with regard to the Botox cost, others will break the price down into the units used. The Botox cost per unit in South Africa is around **R1200**. The amounts of injections required will depend on how much one needs to have done. A consultation with the medical doctor or cosmetic dentist will help determine this.

The cost of Botox injections varies greatly, depending on where one is in South Africa and the professional who is performing the administration. The amount of injections that one receives at one time as well as the practitioner's qualifications will also be reflected in the Botox cost

Practitioners pay for each vial, which unfortunately becomes ineffective after only a few hours after it has been opened. Beyond this time, the vial must be discarded. The Botox cost will be less if one shares the expense of the vial with some friends. So, get the friends together at the practitioner's consulting rooms and have a Botox Party!

Limitations of Botox include:

- The effect is not permanent.
- There is no guarantee the desired effect will be achieved.
- The ageing process will still happen elsewhere – for example, Botox will not fix sagging eyelids.

Disadvantages of Botox - unfortunately, after one has gotten the wonderful result that one was hoping for, it will dissipate. The results are temporary and only last for 3 to 6 months.

Because Botox is a toxin, albeit in dilute form, adverse reactions are possible. These include:

- Nausea
- Headaches
- Tingling
- Bruising
- Swelling at injection sites

Safety – one should take time to find a reputable practitioner who is properly qualified and practises in a clean, safe and appropriate environment. Ask the practitioner what one should do if something were to go wrong.

It is crucial to consider if one is a possible candidate for Botox treatment. People who could not be considered for Botox injections include those who:

- Are taking medications for blood thinning. This would increase bleeding, bruising or blood accumulation at the injection sites
- Have a history of botulism poisoning. These people are vulnerable to recurrence of poisoning at a lower dose
- Are pregnant
- Are Lactating (nursing infants)

Botulinum toxin is a prescription-only medicine that should only be prescribed and given by an appropriately trained healthcare professional, such as a doctor or dentist. Legally, the prescriber can

delegate the administration of the injections to another person, but they remain responsible for ensuring it is given safely.

Women should not have botulinum injections if pregnant or breastfeeding, since the effects on the foetus or baby are not known.
(Cosmetic Dentistry).

Botox Use by Cancer Survivors

According to Dr Ronald Shelton, MD (a Manhattan Dermatologic Surgeon) chemotherapy is not a contraindication to undergo Botox and fillers treatment. It is, however, good to discuss this with one's oncologist prior to going for Botox treatment. If the oncologist agrees, then it can be done.

Some individuals might have very intense chemotherapy that may interfere with their defences against infection and then possibly a slightly greater risk of infection would occur from having fillers, but this still would be rare.

It is important for those who are having chemotherapy, to maintain as optimistic a view as possible and feeling better about themselves during the treatment – this may help their immune system cope. They should not feel guilty having an aesthetic treatment during such an important treatment as chemotherapy, but feel rather, that the aesthetic treatment is an adjunct to treating their whole person and helping them progress through and complete the chemotherapy and increasing their odds of getting a remission.

The Future: Botox and Cancer Treatment

Botox and cancer pain - a group of researchers studied the effect of onabotulinumtoxinA in seven cancer patients who suffered from severe focal pain (visual analog scale >5) at the site of local surgery or radiotherapy or both. OnabotulinumtoxinA (20-100 units) was injected into the focal pain areas (skin or muscle or both). Five of seven patients were followed beyond 1 year (1.5-5 years) with repeat treatment.

All seven patients reported a significant improvement in pain (mean drop in visual analog scale score of 5.1). They described their response on the patient global assessment as satisfactory (two patients) or very satisfactory (five patients).

Six of seven patients found the pain relief associated with significant improvement in quality of life. One patient developed weakness of jaw muscles after bilateral masseter injection that was not observed during second injection (reduced dose). Improvements with treatment persisted with repeat injections during long-term follow-up (five patients).

Local treatment with onabotulinumtoxin A can significantly reduce pain and improve quality of life in cancer patients suffering from pain in the area of surgery and radiation and was well tolerated in cancer patients.
(Mittal, Machado & Jabbari, 2012).

Botox and nerve pain in cancer patients - neuropathy, a type of pain caused by nerve damage, is not a uniform condition but instead may appear in different forms. Botox might offer effective relief for two forms of neuropathy, a new animal study finds. In fact, botulinum toxin produced a lasting reduction of pain in mice suffering from either physical or chemotherapy-related nerve injury.

Cancer patients often experience a pain known as chemotherapy-induced peripheral neuropathy. The peripheral nerves carry sensations (feeling) to the brain and control the movement of our arms and legs. They also control the bladder and bowel. The chemotherapy drugs cisplatin, carboplatin, and oxaliplatin, though, may damage these nerves. Symptoms may include either shooting pain or a loss of feeling in the hands and feet. Sometimes what should be cold to the touch will cause a burning sensation instead.

For many cancer patients, the symptoms disappear over time. Others, unfortunately, are not so lucky. Past research has shown Botox can treat some forms of chronic pain. (Park & Park, 2017).

Botox and cancer cell growth – another study has shown that cancer growth could be suppressed by eliminating the signals sent by nerves that are linked to cancer stem cells. The approach thus treated the cancer. The use of Botox made the treatment cheap, safe and efficient. The researchers have tested the procedure on mice, and will soon start testing on humans.

The nervous system is crucial in regulating many organs. Researchers from the Norwegian University of Science and Technology (NTNU), Columbia University and MIT, along with researchers from Japan and Germany have now shown that the vagal nerve contributes to the growth of gastric tumours, so that stopping the nerve signal to the tumour will stop its growth.

“This study shows that nerves control cancer stem cells,” say NTNU Professor Duan Chen and Columbia Professor Timothy Wang, the co-corresponding authors of the study published in *Science Translational Medicine*.

“We found that by removing the effect of the nerve, the stem cells in the cancer tumour are suppressed, leading to cancer treatment and prevention,” Chen says.

This study found that nerves promote tumour growth through the release of a neurotransmitter. (ScienceNordic).

Botox and prostate cancer - Botulinum toxin type A (BTA) intraprostatic (into the prostate gland) injection induces an improvement of urinary symptoms related to benign prostatic hypertrophy (BPH). Infra-clinical prostate cancer (PCa) foci and pre-neoplastic lesions occur concomitantly with BPH in a significant number of patients. The objective of this study was to address whether BTA influences the growth of prostate tumours.

BTA significantly reduced LNCaP cell proliferation and increased apoptosis in a dose-dependent manner but did not affect PC-3. The SV2 receptor was present in both cell lines at a ratio of 4:1 (LNCaP/PC-3). One unit of BTA resulted in a significantly lower growth rate and slower PSA progression over 28 days compare to controls. The tumours were morphologically similar. There were significantly more apoptotic cells compared to controls.

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BTA inhibits the growth of LNCaP human PCa cells in vitro and in vivo. These findings indicate that intra-prostatic BTA injections to treat BPH are unlikely to promote the growth of co-existing infra-clinical PCa foci in men. A potential inhibitory effect of BTA on the growth of human PCa should be further studied.

(Karsenty, *et al.*, 2009).

Use of botox for radiation-induced head and neck pain:

Mailly, M., Bensakin, S., Chauvin, A., Brasnu, D. & Avache, D. 2019.

Purpose: To report the results of Botulinum Toxin A (BTA) for radiation-induced head and neck pain.

Materials and methods: This single-center retrospective study included all the patients treated at our institution with botulinum toxin A injections for radiation-induced head and neck pain between 2006 and 2017. Pain was evaluated by each patient on a visual analogue scale (VAS) (between 0 and 10) before, and 1 month after the injection.

Results: Sixteen patients were included in this series. The mean value of the pain was 8.5 before and 8 after the first injection. The difference was statistically significant ($p < 0.01$). Major response occurred in 15 patients ($VAS \leq 3$ after BTA) and complete response in 11 patients ($VAS = 0$ after BTA).

Conclusion: Botulinum toxin is an effective treatment for radiation-induced head and neck pain.

Use of botox to preserve gland function after radiotherapy in patients with head and neck cancer:

Teymoortash, A., Pfestroff, A., Wittig, A., Franke, N. Hoch, S., Harnisch, S., Schade-Brittinger, C., Hoeffken, H., Engenhardt-Cabillic, R., Brugger, M. & Strauch, K. 2016.

“This prospective, randomized, placebo-controlled, double-blinded phase I clinical trial investigates safety and efficacy of botulinum toxin (BoNT) to preserve gland function after radiotherapy in patients with head and neck cancer. Twelve patients with advanced head and neck cancer were injected with BoNT into the submandibular glands prior to primary radiochemotherapy. Six patients received BoNT/A and 6 patients BoNT/A and B, half of each subgroup into their left and the other half into their right gland. As an internal control, sodium chloride was injected into the respective contralateral gland (placebo). For the evaluation of the salivary gland function, technetium pertechnetate salivary gland scintigraphy was performed before and after the end of radiotherapy. BoNT/A and B were well tolerated. Analysis of the scintigraphic data revealed no statistically significant difference between BoNT and placebo regarding the scintigraphic uptake difference ($p_{BoNT/A} = 0.84$ and $p_{BoNT/A-B} = 0.56$ for BoNT/A vs. placebo and BoNT/A-B vs. placebo, respectively). We also found no significant difference in treatment between BoNT and placebo in terms of salivary excretion fraction ($p_{BoNT/A} = 0.44$; $p_{BoNT/A-B} = 0.44$). This study demonstrates that BoNT can be safely combined with radiochemotherapy. Dosing and timing of BoNT injection should be further investigated for efficacy analysis. Trial Registration German Registry for Clinical Trials DRKS00004595.”

Use of botox as primary treatment for strabismus in patients with nasopharyngeal carcinoma related to sixth nerve palsy:

Wong, E.A., Lam, C.P.S., Lau, F.H.S., Lau, W.W.Y. & Yam, J.C.S. 2018.

Purpose: The purpose of this study is to evaluate the efficacy and safety of botulinum toxin injection as a primary treatment for strabismus in a cohort of patients with nasopharyngeal carcinoma (NPC)-related chronic sixth nerve palsy.

Patients and methods: We retrospectively reviewed all cases of NPC-related sixth nerve palsy receiving botulinum toxin injection in the Hong Kong Eye Hospital between January 2009 and January 2016. Only cases with diplopia for at least 6 months; and failed a trial of Fresnel prism therapy were recruited. We excluded cases with prior strabismus surgery and multiple cranial nerve palsies. Patients were offered botulinum toxin injection as primary treatment for their strabismus and were given further injections or offered surgery if diplopia persisted. Success with botulinum toxin was defined as a final distant orthophoria of <15 PD in primary gaze, no diplopia in primary position, and no head turn, as measured 6 months after the last injection, without requiring a second treatment.

Results: A total of 25 patients were included in the study. All patients received concurrent chemoradiotherapy for NPC. There was a statistically significant reduction in the mean deviation at distant after the last injection compared to that at presentation ($P < 0.001$, Wilcoxin signed rank test). Overall, 7 patients (28%) achieved clinical success and 15 patients (64%) remained diplopia-free by repeated botulinum toxin injections alone. Nine patients went on to receive definitive surgery and all achieved good ocular alignment after surgery. Transient ptosis or vertical deviation was seen in 7 patients, which resolved within 3 months and no serious complications arose from the treatment in our series.

Conclusions: Botulinum toxin injection is a relatively less-invasive alternative to surgery that can be done under a topical anesthesia setting, which improves patient's quality of life via reduction in diplopia. It is a recommendable initial option in patients with chronic nerve palsies who may have higher risks associated with strabismus surgery.

Effectiveness of botox use in patient with persistent upper limb pain in breast cancer survivors:

De Groef, A., Devoogdt, N., Van Kampen, M., Nevelsteen, I., Smeets, A., Neven, P., Geraerts, I., Dams, L., Van der Gucht, E. & Debeer, P. 2018.

Objective: To investigate the effect of a single botulinum toxin A (BTX-A) infiltration in the pectoralis major muscle in addition to a standard physical therapy program for treatment of persistent upper limb pain in breast cancer survivors.

Design: Double-blinded (patient and assessor) randomized controlled trial.

Setting: A university hospital.

Participants: Breast cancer patients (N=50) with pain.

Intervention: The intervention group received a single BTX-A infiltration. The control group received a placebo (saline) infiltration. Within 1 week after the infiltration, all patients attended an individual physical therapy program (12 sessions) during the first 3 months and a home exercise program up to 6 months after infiltration.

Main outcome measures: The primary outcome was change in pain intensity at the upper limb (visual analog scale, 0-100) after 3 months. Secondary outcomes were prevalence rate of pain, pressure hypersensitivity, pain quality, shoulder function, and quality of life. Measures were taken before the intervention and at 1, 3, and 6 months' follow-up.

Results: No significant difference in change in pain intensity after 3 months was found (mean difference in change, 3/100; 95% confidence interval [CI], -13 to 19). From baseline up to 6 months, a significantly different change in upper limb pain intensity was found between groups in favor of the intervention group (mean difference in change, 16/100; 95% CI, 1-31).

Conclusions: A single BTX-A infiltration in combination with an individual physical therapy program significantly decreased pain intensity at the upper limb in breast cancer survivors up to 6 months. However, the effect size was not clinically relevant, and no other beneficial effects were found.

Medical Disclaimer

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