Medical Science Journal for Advance Research

Vol. 6, No. 4, December 2025
e-ISSN: 2774-4892

Botulinum Toxin: The Hopeful Prospects for Treating Prostate Cancer

Marwa H. Almuhammady *[1], Zahraa Abdul-Hussain AL-Moomen [2] and Sarah Ali Aljazaeri [3]

[1,3] *University of Kufa, College of Science, Iraq.*
[2] *Ministry of Education, Najaf, Iraq.*
***Corresponding Author Email:** *marwaha.almuhammady@uokufa.edu.iq, zahraaalmoomen2@gmail.com, saraha.aljazaeri@uokufa.edu.iq

ABSTRACT

It has been demonstrated that peripheral nerves influence the development and metastasis of prostate tumors by supplying nourishment to the stroma and cancer cells within the tumor environment. The impact of botulinum toxin (BT) on prostate tumor tissue has been documented in a number of in vitro and in vivo investigations. Human BT has been shown to induce cancer cell death, resulting in morphological alterations that include large atrophic and degenerative cancerous regions, decreased pyknotic nuclei and cytoplasm compared to cancer tissues injected with saline Experimental, epidemiological, and clinical evidence showing the impact of BT in the management of prostate cancer has been produced using this body of knowledge about physiology and pathology. This suggests a potent treatment plan , that would lower prostate cancer mortality.

Keywords: Botulinum Toxin (BT), Prostate Cancer, Peripheral Nerves, Tumor, Cancer Cell Death , Microenvironment.

Article Information
Received: November 07, 2025; Revised: December 09, 2025; Online: December 2025

INTRODUCTION

The bacterium Clostridium Botulinum and similar species produce the powerful neurotoxin known as botulinum toxin (BT) [1]. It works by desensitizing sensory nerves and preventing acetylcholine from being released, which inhibits neuromuscular connections. Its effects when administered to the prostate extend beyond the neuromuscular junction to the neuroglandular junction [2]. [3] were the first to disclose the use of BT in the prostate. They examined its effects in 30 rats and discovered diffuse glandular apoptosis and widespread acinar cell atrophy. Two follow-up experiments in rats and dogs, respectively, confirmed this effect [4,5].

[4] reported A detrimental control of alpha1A-adrenergic receptors in the rodent prostate minus alterations Regarding androgen receptors, and [6] verified the effect of widespread atrophy of glandular cells collected before and after injection of BT in humans. Prostatic involution can be induced by BT without resulting in severe systemic side effects or local inflammation. This should encourage more studies on its effects on benign and malignant prostate lesions. Based on available data, well-designed clinical trials that test its effects on prostate cancer can be proposed [2] as in **Fig. (1)**.

https://doi.org/10.46966/msjar.v6i4.331

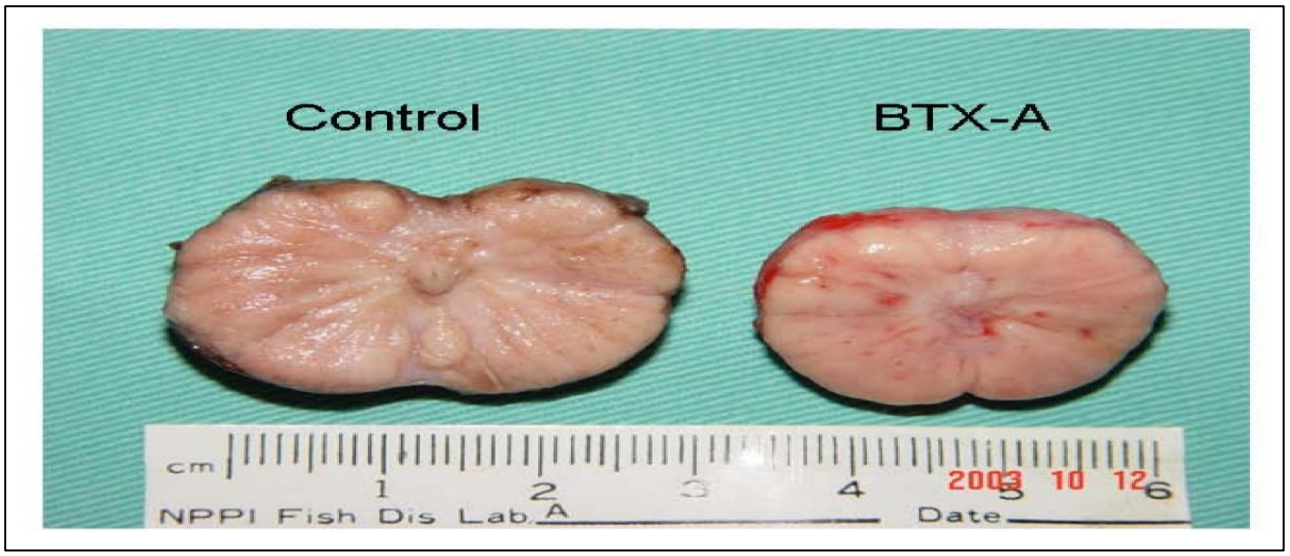


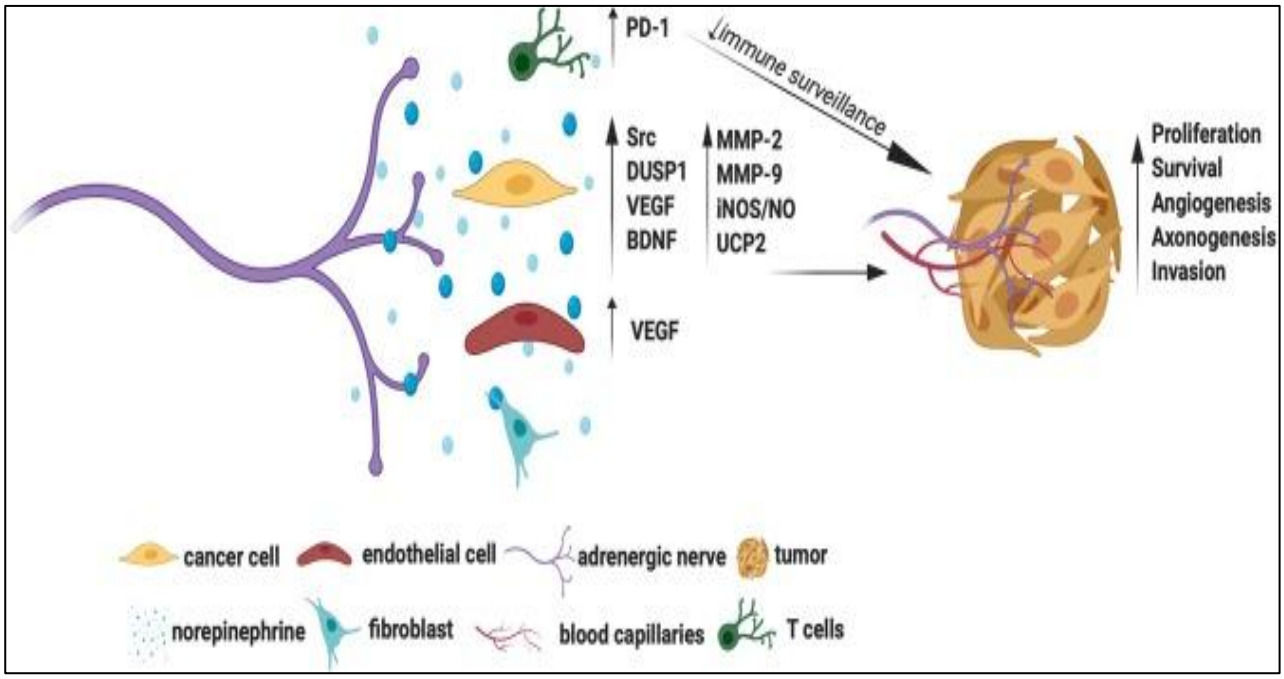
Fig. (1): Coronal section of canine prostate one month after BTX-A or saline injection. Smaller in size and less indurations after BTX-A injection (B) than the control (A).[32].

Neural Impact on the Development of Prostate Cancer.

Not only are nerves implicated in embryological development of the pelvic floor, but they are also associated with controlling the prostate [7]. There was a long period where nerves were not considered pain transporters at all, as in the instance of the tumoral prostate and that of the healthy prostate homeostasis [8]. But, the stroma and cancer cells in the tumour microenvironment are innervated by peripheral nerves that may regulate tumor development and metastasis [9][10][11]as in fig. (2).

The existence of neurological dependence of cancers was first discovered in the invasion perineural, where cancer cells travel along and invade nerves [12] Perineural invasion had long been recognized as a physical connection between cancer cells and nerves, but it has only been in the past 20 years that experimental models have demonstrated that cancer cells promote growth of neurons. According to reference [9], infiltrating nerves offer molecular assistance that promotes tumor development and spread. Infiltration stalk for their part, guides the invasion of tumorigenic cells. When grown together, prostate cancer cells were beneficial for the development and direction of sensory neurons and vice versa. [13] The stimulation of adrenergic impulses by stress enhances tumor growth, indicating the important contribution of the sympathetic nervous system to tumorigenesis. Signals that are adrenergic in nature found in stromal cells are but crucial for the development of tumors.

In addition, the absence of cholinergic signals in stromal cells inhibits the spread of (prostate cancer). The innervation of prostate cancer is probably triggered by neurotrophic growth factor along with The purpose of neural progenitor cells derived from the brain. This factor is secreted by tumor cells. Prostate cancer induces neurogenesis and axonogenesis. The first stage of this development is called precancerous high-grade prostatic intraepithelial neoplasia [17]. In addition, perineural invasion gives nerve cancer contacts a survival advantage to cancer cells[18].



Molecular mechanisms for the tumor promoting actions of adrenergic signals [33].

Botulinum Toxin as a Medicinal Substance

This set of data, which contains physiological and pathologic information, has produced clinical, epidemiological and experimental finding. In this way, BT may help control prostate cancer, which could be an effective therapy to cut many death rates from prostate cancer.

Mice experts and Patrick Cassy discovered that botulinum toxin therapy slows down the growth of prostate cancer cells in vitro and in vivo. BT decreased LNCaP cells' growth and apoptosis was increased in a dose dependent manner. performed similar experiments with the PC3 and LNCaP lines and showed that dosages of BT of 15 U/mL decreased the mitotic index [20].

Additionally, phosphorylated phospholipase A2 (PLA2) expression was elevated by botulinum toxin. It has been proposed that BT-A suppresses the manifestation of engaged PLA2, which might lessen a production of arachidonic acid and eicosanoids. Eicosanoid byproducts of a lipoxygenase (LOX) and Cyclo-oxygenase (COX) routes, which also regulate tumor vascularization and metastasis in animal models, play a major role in the proliferation of prostate cancer cells in culture. Pharmacological treatments that can stop the growth of prostate cancer xenografts by restricting either COX or LOX products. Recent research has shown that PLA2 enzymes regulate the production of prostate cancer cells and tumors. in addition to controlling the availability of arachidonic acid to eicosanoids produced by COX and LOX [21]. In nearly all cases of human prostate cancer, secretory PLA2 is overexpressed tissues, and higher tumor grade is linked to higher amounts of this protein [22]. It makes sense that in addition to inducing neoplastic cells to undergo apoptosis, BT may also affect factors that promote tumor growth. [23] demonstrated that human BT treatment increased the mortality of tumor cells on the BT-treated side, at p=0.0020.Spinal cord injury patients, BT-treated patients and tumors arising in denervated rodent prostates all shared a similar denervation gene array profile. A unique genetic profile of the induced denervation suggested translation and bioenergetic halt. When the BT-injected side of the tissue excised following the prostatectomy was compared to the saline-injected side, The former showed distinctive morphological features of pyknotic nuclei, scant

cytoplasm, and extensive features of cancer atrophy and degeneration, while the latter showed apoptotic cancer cells in areas of neural invasion. No appreciable change in proliferation, as evidenced by Ki67 staining, was observed.

BT Treatment Safety and Clinical Results

One noteworthy point with possible therapeutic applications Is the utilization of BT as an adjuvant for radiation or chemotherapy. In animal tumors (fibrosarcoma and hepatocarcinoma), local BT type A treatment significantly improves tumor oxygenation and perfusion, with a significant improvement in the tumor's response to radiation (20 Gy of 250 kV) and chemotherapy (cyclophosphamide, 50 mg/kg) [24]. The therapeutic benefit claimed is due to BT type A opening the tumor vascular bed by suppressing The tumor's neurogenic tone vasculature. A man with metastatic prostate cancer who's 68 years old, had a Gleason score of 4 + 4 = 8, 521 ng/mL of baseline blood PSA, and severe bone disease. The only localized hypoechoic area found by transrectal ultrasonography received an intraprostatic transperineal shot of BT type A using 1,000, units of DysportTM/ Ipsen, dissolved in the water a 0.5% solution adrenaline infusion [25]. The blood PSA level dropped up to 101 ng/mL, the prostate's total volume shrank from 48.8 to 34.3 cm^3 (30% reduction) two months after BT treatment, as well as prostate transrectal ultrasonography ,revealed no hypoechoic lesions. In spite of The possible adverse effects of using BT local, there is adequate Clinical evidence shows that the medicinal use of BT is safe and simple into perform [26]. Installments were infrequent and seemed related more to urethral manipulation (acute prostatitis, temporary urine retention, and severe hematuria) than the injection of BT itself [27]. Acute prostatitis was the only reported side effect of BT injection in a 2-year follow-up by Rodrigues et al. [28]. The toxin can theoretically be absorbed systemically because of the vascular nature of the prostate. No systemic adverse effects have been reported following intraprostatic injections even with doses as large as 300 U of BT [29]. Since the diffusion of BT from its injection site is known to be at least partly dependent on a receptor's active binding component, The size and shape of the diffusion halo may vary either on gland surfaces or nerve terminals, depending on the number of receptors [30]. The injection applied in the prostate of botulinum toxin does not impact wish or erectile, orgasmic, or ejaculatory function [31]. Though further research is needed to clarify the mechanisms of action of BT on malignant tumor cells in the prostate, Research to explore the impact of BT on prostate cancer ought to be advanced.

CONCLUSION

BT produces continuously impacts the growth and expansion of prostate cancer, encouraging research on its usage as a treatment will allow findings that result in new techniques for therapy.

REFERENCES

1. Montecucco C, Molgó J. Botulinal neurotoxins: revival of an old killer. Current Opinion in Pharmacology. 2005 Jun 1;5(3):274-9.

2. Morales AP, Marrero DF. Effects of botulinum toxin on the glandular portion of the prostate: pathophysiological foundations, mechanism of action and evidence. Mexican Journal of Urology. 2020 Sep 1; 80 (4): 1-10.

3. Doggweiler R, Zermann DH, Ishigooka M, Schmidt RA. Botox-induced prostatic involution. The Prostate. 1998 Sep 15;37(1):44-50.

4. Chuang YC, Huang CC, Kang HY, Chiang PH, Demiguel F, Yoshimura N, et al. Novel action of botulinum toxin on the stromal and epithelial components of the prostate gland. The Journal of Urology. 2006 Mar;175(3):1158-63.

5. Chuang YC, Tu CH, Huang CC, Lin HJ, Chiang PH, Yoshimura N, et al. Intraprostatic injection of botulinum toxin type-A relieves bladder outlet obstruction in human and induces prostate apoptosis in dogs. BMC Urology. 2006 Dec;6(1):1-6.
6. Kuo HC, Liu HT. Therapeutic effects of add-on botulinum toxin A on patients with large benign prostatic hyperplasia and unsatisfactory response to combined medical therapy. Scandinavian Journal of Urology and Nephrology. 2009 Jan 1;43(3):206-11.
7. Bitoh Y, Shimotake T, Sasaki Y, Iwai N. Development of the pelvic floor muscles of murine embryos with anorectal malformations. Journal of Pediatric Surgery. 2002 Feb 1;37(2):224-7.
8. Galán ML, Borda AP, González LL, Sánchez AB. Effect of sacral roots block in the prostatic structure of the rat. Actas Urologicas Espanolas. 2000;24(7):516-21.
9. Bautista M, Krishnan A. The autonomic regulation of tumor growth and the missing links. Frontiers in Oncology. 2020 May 13;10: 744.
10. Jobling P, Pundavela J, Oliveira SM, Roselli S, Walker MM, Hondermarck H. Nerve–cancer cell cross-talk: a novel promoter of tumor progression. Cancer Research. 2015 May 1;75(9):1777-81.
11. Boilly B, Faulkner S, Jobling P, Hondermarck H. Nerve dependence: from regeneration to cancer. Cancer Cell. 2017 Mar 13;31(3):342-54.
12. Li R, Wheeler T, Dai H, Ayala G. Neural cell adhesion molecule is upregulated in nerves with prostate cancer invasion. Human Pathology. 2003 May 1;34(5):457-61.
13. Ayala GE, Wheeler TM, Shine HD, Schmelz M, Frolov A, Chakraborty S, et al. In vitro dorsal root ganglia and human prostate cell line interaction: redefining perineural invasion in prostate cancer. The Prostate. 2001 Nov 1;49(3):213-23.
14. Thaker PH, Han LY, Kamat AA, Arevalo JM, Takahashi R, Lu C, et al. Chronic stress promotes tumor growth and angiogenesis in a mouse model of ovarian carcinoma. Nature Medicine. 2006 Aug;12(8):939-44.
15. Magnon C, Hall SJ, Lin J, Xue X, Gerber L, Freedland SJ, et al. Autonomic nerve development contributes to prostate cancer progression. Science. 2013 Jul 12;341(6142).
16. March B, Faulkner S, Jobling P, Steigler A, Blatt A, Denham J, et al. Tumour innervation and neurosignalling in prostate cancer. Nature Reviews Urology. 2020 Feb;17(2):119-30.
17. Olar A, He D, Florentin D, Ding Y, Ayala G. Biologic correlates and significance of axonogenesis in prostate cancer. Human Pathology. 2014 Jul 1;45(7):1358-64.
18. Ayala GE, Dai H, Tahir SA, Li R, Timme T, Ittmann M, et al. Stromal antiapoptotic paracrine loop in perineural invasion of prostatic carcinoma. Cancer Research. 2006 May 15;66(10):5159-64.
19. Karsenty G, Rocha J, Chevalier S, Scarlata E, Andrieu C, Zouanat FZ, et al. Botulinum toxin type A inhibits the growth of LNCaP human prostate cancer cells in vitro and in vivo. The Prostate. 2009 Aug 1;69(11):1143-50.
20. Proietti S, Nardicchi V, Porena M, Giannantoni A. Attivita della tossina botulinica A in linee cellulari di cancro prostatico. Urologia. 2012 Apr 1;79(2):135-41.
21. Dong Q, Patel M, Scott KF, Graham GG, Russell PJ, Sved P. Oncogenic action of phospholipase A2 in prostate cancer. Cancer Letters. 2006 Aug 18;240(1):9-16.
22. Dong Z, Liu Y, Scott KF, Levin L, Gaitonde K, Bracken RB, et al. Secretory phospholipase A2-IIa is involved in prostate cancer progression and may potentially serve as a biomarker for prostate cancer. Carcinogenesis. 2010 Nov 1;31(11):1948-55.
23. Coarfa C, Florentin D, Putluri N, Ding Y, Au J, He D, et al. Influence of the neural microenvironment on prostate cancer. The Prostate. 2018 Feb;78(2):128-39.
24. Baudelet C, Cron GO, Dessy C, Martinive

P, De Wever J, Verrax J, et al. Botulinum toxin potentiates cancer radiotherapy and chemotherapy. Clinical Cancer Research. 2006 Feb 15;12(4):1276-83.
25. Vezdrevanis K. Prostatic carcinoma shrunk after intraprostatic injection of botulinum toxin. Urology journal. 2011 Jul 1;8(3):239-41.
26. Mostachio GQ, Apparício M, Motheo TF, Alves AE, Vicente WR. Intra-prostatic injection of botulinum toxin type A in treatment of dogs with spontaneous benign prostatic hyperplasia. Animal Reproduction Science. 2012 Aug 1;133(3-4):224-8.
27. Arnouk R, Suzuki Bellucci CH, Stull RB, de Bessa Junior J, Malave CA, Gomes CM. Botulinum neurotoxin type A for the treatment of benign prostatic hyperplasia: randomized study comparing two doses. The Scientific World Journal. 2012 Sep 10;2012: 463574.
28. de Carvalho TG, Pinto R, Cruz F, Silva J. Effect of onabotulinum toxin type a intraprostatic injection on the outcome of Benign Prostatic Hyperplasia patients refractory to medical therapy: A 2-year follow-up study. Spanish Archives of Urology. 2016; 69 (10): 719-26.
29. Park DS, Cho TW, Lee YK, Lee YT, Hong YK, Jang WK. Evaluation of short-term clinical effects and presumptive mechanism of botulinum toxin type A as a treatment modality of benign prostatic hyperplasia. Yonsei Medical Journal. 2006 Oct 31;47(5):706-14.
30. Hexsel DM, Soirefmann M, Rodrigues TC, do Prado DZ. Increasing the field effects of similar doses of Clostridium botulinum type A toxin–hemagglutinin complex in the treatment of compensatory hyperhidrosis. Archives of Dermatology. 2009 Jul 1;145(7):837-40.
31. Silva J, Pinto R, Carvalho T, Botelho F, Silva P, Silva C, et al. Intraprostatic botulinum toxin type A administration: evaluation of the effects on sexual function. BJU international. 2011 Jun;107(12):1950-4.
32. Yao-Chi Chuang, Chieh-Hsien Tu, Chao-Cheng Huang, Hsin-Ju Lin, Po-Hui Chiang, et al. Intraprostatic injection of botulinum toxin type- A relieves bladder outlet obstruction in human and induces prostate apoptosis in dogs. BMC Urology volume 6, Article number: 12 (2006).
33. Maricris Bautista , Anand Krishnan, The Autonomic Regulation of Tumor Growth and the Missing Links. National Center for Biotechnology Information , 2020 May 13;10:744. doi: 10.3389/fonc.2020.00744

