Archives in Cancer Research©
3 (11) 2023 : 001-003 • REVIEW ARTICLE

Docetaxel resistance in prostate cancer

Shinu Ozaki*

Department of Urology, Republic of Korea

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

ABSTRACT

Prostate cancer is one of the most common malignant tumours in the world, and it can occur as a result of genetic mutations and their accumulation when the tumour progresses to an advanced stage. Because of the absence of distinct symptoms in the early stages of prostate cancer, most cancer patients are discovered at advanced stages where tumour cells respond poorly to chemotherapy. Furthermore, genetic alterations in prostate cancer increase tumour cell aggressiveness. Docetaxel and paclitaxel are well-known drugs for prostate tumour treatment, and they have a similar role in cancer therapy that is based on preventing depolymerization of microtubules, disrupting microtubule equilibrium, and causing a delay in cell cycle progression. The current review seeks to provide insight on the mechanisms behind paclitaxel and docetaxel resistance in prostate cancer. When oncogenic factors such as CD133 are upregulated and PTEN, a tumour suppressor, is downregulated, prostate tumour cells become more malignant and can develop medication resistance. Furthermore, phytochemicals have been used as anti-tumor agents to reduce chemoresistance in prostate cancer. Naringenin and lovastatin are two anti-tumor drugs that have been utilised to slow the development of prostate cancer and improve treatment sensitivity. Furthermore, nanostructures like polymeric micelles and nanobubbles have been used to deliver anti-tumor drugs while reducing the danger of chemoresistance development. The current review highlights these topics in order to bring fresh insight on reversing treatment resistance in prostate cancer.

Keywords: Prostate cancer, Paclitaxel, Docetaxel, Chemoresistance, Targeted delivery, Nanoparticles

Address for correspondence:

Shinu ozaki,
Department of Urology, Republic of Korea
E-mail: ozakishinu@rediff.com

Word count: 1570 **Tables:** 00 **Figures:** 00 **References:** 10

Received: 02.05.2023, Manuscript No. ipacr-23-13686; **Editor assigned:** 04.05.2023, PreQC No. P-13686; **Reviewed:** 18.05.2023, QC No. Q-13686; **Revised:** 23.05.2023, Manuscript No. R-13686; **Published:** 30.05.2023

INTRODUCTION

Prostate cancer is the most frequent non-cutaneous tumour among males in the United States. Docetaxel is a good chemotherapeutic medication for prostate cancer that has been available for over a decade, but the length of therapy and systemic side effects make it difficult to adhere to. Furthermore, docetaxel resistance inevitably develops, resulting in disease recurrence. Docetaxel resistance can be innate or acquired through a variety of processes that are strongly linked to genetic changes, reduced drug inflow, and enhanced drug efflux. To boost the therapeutic potential of docetaxel in prostate cancer, several combination treatments including tiny P-glycoprotein inhibitors have been developed. Novel treatment techniques for reversing docetaxel resistance include enzyme modifications, improved drug absorption, and apoptosis augmentation. In this study, we provide the most recent docetaxel reversal techniques that make use of nanotechnology. Docetaxel administration using nanotechnology is superior to conventional treatment techniques and a more effective way for inducing P-glycoprotein inhibition, increasing cellular uptake, maintaining prolonged drug release, and improving bioavailability [1-5].

Prostate cancer is androgen (AR) sensitive in the early stages and can be treated with either an androgen-receptor antagonist or chemical castration; however, as the cancer progresses, the majority of cases become androgen-resistant; response to these treatments is poor, resulting in high rates of mortality and morbidity. Hormone treatment has been widely utilised to treat advanced-stage prostate cancer, and it is also effective in treating androgen-sensitive prostate cancer. After a specific amount of time, the majority of prostate cancer cells gain hormone resistance and become androgen independent. The Food and Drug Administration has authorised docetaxel for the treatment of several metastatic prostate malignancies, including androgen independent and castration resistant prostate cancer. Docetaxel resistance, on the other hand, has been a substantial clinical issue since it was approved as a first-line therapy for metastatic castrate-resistant prostate cancer. Newer chemotherapeutic medicines designed to treat docetaxel-resistant patients have considerable haematological side effects that may outweigh the advantages. As a result, the purpose of this review is to examine new nanotechnology-based techniques and future perspectives for overcoming docetaxel resistance in the treatment of prostate cancer.

Historically, treating metastatic castrate-resistant prostate cancer has been difficult, with few therapeutic results. Docetaxel was the first cytotoxic medication linked to

improved survival in castrate-resistant prostate cancer. Toxicity is consistent with other cytotoxic drugs, with myelosuppression being the dose-limiting toxicity and neurotoxicity being a significant side effect for certain individuals. Unfortunately, many men with castrate-resistant prostate cancer will not respond to docetaxel-based treatment, and all patients will eventually acquire resistance. Docetaxel, despite its risks and limitations, is expected to remain an essential element of the treatment arsenal against metastatic prostate cancer for the foreseeable future since it is an effective medicine. Overcoming docetaxel resistance has been a difficulty since the drug was originally used to treat metastatic castrate-resistant prostate cancer. Several novel medicines, including cabazitaxel and abiraterone, have been proven in recent studies to be beneficial following docetaxel failure, radically shifting the treatment landscape for these patients. Furthermore, a better knowledge of the processes generating docetaxel resistance has led to the development of various innovative therapeutic options that offer promise for the future. This review will go over recent therapy developments as well as ongoing clinical studies in metastatic castrate-resistant prostate cancer [6-10].

CONCLUSION

Docetaxel chemotherapy is quite important in the clinical oncology of prostate cancer. Although this medication has had tremendous success in eradicating tumor(s) or reducing tumor(s) development and spread, it is limited in its usage due to dose-dependent adverse effects and the formation of chemoresistance. The recorded findings provided in this review outline the clinical viability of nanotechnology-mediated docetaxel treatments. Docetaxel nanoformulations combined with multidrug (chemo-sensitizers or synergetic drugs), targeting moiety, siRNA, miRNA, and immunoactivation compositions are good techniques for overcoming drug resistance and evading target tumour cells. Furthermore, because of enhanced drug targeting, higher intracellular accumulation, and prolonged release for superior pharmacological activities, these docetaxel nanoformulations minimise the chemotherapeutic dosage necessary for treatment. These features greatly minimise chemotherapy-related side effects and recurrence. According to the literature, clinically relevant and successful docetaxel nanoformulations for prostate cancer therapy have a suitable particle size (100 nm) and possibly a negative zeta potential, must use safe, proper, and approved technology, identify an appropriate stabilisation step, engineer an accurate targeting moiety, and induce multi-functionality for theranostic purposes. This review demonstrates that different nanoformulations of docetaxel can reverse docetaxel resistance by blocking or modifying whole resistance pathways. Docetaxel nanoparticle administration is both safe and effective in overcoming defective docetaxel delivery and docetaxel resistance. It is also conceivable to combine targeted systemic chemotherapies with nanodocetaxel formulations to improve the docetaxel therapeutic result in prostate cancer by targeting, accumulation, and prolonged release of docetaxel. In our opinion, a biocompatible nanoparticle formulation of docetaxel with controlled release and multifunctionality that can target tumour cells by overexpressing ligands/antigens such as prostate stem cell antigen, prostate specific membrane antigen, six transmembrane epithelial antigen of the prostate 1, prostatic acid phosphatase, T cell receptor gamma alternate reading frame protein, transient receptor potential (trp)-p8, and a specific signalling pathway This formulation will eventually solve the majority of the docetaxel-related challenges and will benefit clinical oncology in the near future.

Chemotherapy is the first-line treatment for prostate cancer, and the most well-known chemotherapeutic drug for this purpose is DTX. Given the similar mode of action of PTX and DTX, PTX is also used to treat prostate cancer by inducing apoptosis and cell cycle arrest. However, treatment failure endangers the lives of many prostate cancer patients over the world. Because DTX and PTX are routinely utilised, considerable research has been directed into studying resistance mechanisms and potential treatment methods for these two anti-cancer drugs. Chemotherapy resistance in prostate cancer is caused by the activation of oncogenic pathways such as STAT3, NF-B, -catenin, and EHZ2, whereas tumor-suppressor proteins such as PTEN are lowered in expression. Non-coding RNAs, such as miRNAs, lncRNAs, and circRNAs, control how prostate cancer cells respond to PTX and DTX treatment. More research on the involvement of circRNAs in PTX resistance in prostate cancer is needed. Given the identification of the underlying molecular processes implicated in PTX and DTX resistance in prostate cancer, blockage of these pathways, such as Notch and JAK1 signalling, resulted in drug sensitivity in prostate tumour cells. As a result, investigations on the use of gene therapy in clinical trials for the treatment of prostate cancer patients are required. Notably, anti-cancer substances such as quercetin and artesunate, among others, have been utilised to slow the growth of prostate cancer, including cell death and chemo-sensitivity. One of the most significant gaps, however, is the lack of targeted administration of phytochemicals for improving chemo-sensitivity in prostate cancer. This is due in part to the low bioavailability of plant-derived natural compounds, which requires further research. Another limitation of used therapies for reversing PTX and DTX resistance in prostate cancer is that studies have ignored using small molecules in reversing drug resistance, instead focusing on phytochemicals. Future studies should focus on using small molecules in prostate cancer therapy. Nano-platforms have emerged as promising new therapeutic possibilities for prostate cancer medication resistance. The first advantage of nanoparticles is that they increase drug accumulation in tumour cells. However, this can enhance the cytotoxicity of PTX and DTX. In the synergistic therapy of prostate cancer, nanostructures can also facilitate the co-delivery of medicines and genes with PTX or DTX. Finally, they may be customised with ligands to target prostate cancer cells specifically. The present investigations are intriguing because they have identified the underlying processes that contribute to the development of PTX and

DTX resistance in prostate cancer and have employed therapeutic techniques to reverse chemo-resistance. However, because PTX and DTX are commonly used in clinical trials in patients for chemotherapy, it is suggested that currently introduced therapeutics for reversing drug resistance or boosting efficacy in cancer chemotherapy be used in patients in the near future while taking safety and biocompatible profiles into account.

REFERENCES

1. **Calò V, Migliavacca M, Bazan V, et al**. STAT proteins: from normal control of cellular events to tumorigenesis. *J Cell Physiol*. 2003; 197 (6):157–68.
2. **Huang D, Chen X, Zeng X, et al**. Targeting the regulator of G protein signaling 1 in tumor-specific T cells enhances their trafficking to breast cancer. *Nat Immunol*. 2021; 22:865–879.
3. **Lu T, Bankhead A, Neamati N, et al**. Multi-omics profiling reveals key signaling pathways in ovarian cancer controlled by STAT3. *Theranostics*. 2019; 9(1):5478–5496.
4. **Robson M, Im SA, Senkus E, et al**. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*. 2017; 377 (7):523–533.
5. **Chang SJ, Hodeib M, Chang J, et al**. Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. *Gynecol Oncol*. 2013; 130(7):493–498.
6. **Gao B**. Cytokines, STATs, and liver disease. *Cell Mol Immunol*. 2005; 2(6):92–100.
7. **Machida K, Tsukamoto H, Liu JC, et al**. C-jun mediates hepatitis c virus hepatocarcinogenesis through signal transducer and activator of transcription 3 and nitric oxide-dependent impairment of oxidative DNA repair. *Hepatology*. 2010; 52 (8):480–492.
8. **Darnell JE Jr., Kerr IM, Stark GR**. Jak-STAT pathways and transcriptional activation in response to IFNs and other extracellular signaling proteins. *Sci.* 1994; 264(4):1415–1421.
9. **Groen RS, Gershenson DM, Fader AN**. Updates and emerging therapies for rare epithelial ovarian cancers: one size no longer fits all. *Gynecol Oncol*. 2015; 136 (6):373–383.
10. **Siegel RL, Miller KD, Fuchs HE, et al**. Cancer statistics, 2022. *CA Cancer J Clin.* 2022; 72(4):7-33.