Prostate cancer and selective serotonin reuptake inhibitors

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EDITORIAL

The prostate gland is largest male accessory sex gland located in the pelvis beneath the urinary bladder and surrounds the prostatic part of urethra. It has fibro-musculo-glandular structure. The prostate gland contains peripheral, central, transitional, periurethral zone and fibromuscular stroma occupies the anterior surface. These zones are made up of many tiny glands which are connected by tiny ducts. Both glands/acini and ducts are lined by secretory epithelium. Beneath the secretory epithelium there is presence of a layer of basal cells and interspersed endocrine-paracrine cells. The peripheral zone form the apex, posterior and lateral part of gland. The peripheral zone form about 70% of the glandular tissue and is most susceptible to prostate cancer (PC). PC is a malignant or uncontrolled growth of the glandular cells of the prostate. PC is one of the most common cancers in the male and the second most common cause of all cancer–related deaths. Most cases of PC are diagnosed in men over 50 years of age. PC is treatable if diagnosed in early stages. the risk of PC development and progression increase after the use of testosterone replacement therapy (TRT) in old age for androgen deficiency or for hypogonadism.

The explanation of this may be that secretory cells of glandular epithelium convert testosterone and adrenal androgens to dihydrotestosterone (DHT) by enzyme 5α-reductase. DHT is about 30 times more potent than testosterone. The growth and proliferation of the prostatic glandular epithelium and androgen dependent prostate cancer is stimulated by the DHT hormone. DHT bind to Androgen receptors (AR) and produce conformational changes of the AR. Then DHT relocate from the cytosole to the cell nucleus and affect cell function. The primary function for AR is direct up- or down regulation of specific gene transcription (1). This also explain why the hormone treatment in the form of Androgen Deprivation Therapy (ADT), or androgen suppression therapy, slow down and even stop cancer growth by reducing androgen levels.

Previous studies on experimental animals showed that selective serotonin reuptake inhibitors (SSRIs) remain useful for the treatment of PC. The uptake of radiolabel analogue of serotonin by the PC cell lines and growth of subcutaneous, PC-3 xenografts in authymic nude mice was significantly inhibited by fluoxetine (2). Fluoxetine is a prototype drug of SSRIs.

Fluoxetine also reported to retard testicular development, decrease the number of Leydig cells, Sertoli cell and germinal cell series in male rats. Testosterone is secreted by interstitial cells of Leydig. Decreased number of Leydig cells leads to decreased level of testosterone (3). Decreased level of testosterone leads to decreased level of DHT and its harmful effects in the form of PC.

SSRIs may also be helpful in PC by increasing serotonin level. Serotonin (5-hydroxy tryptamine, 5-HT) exerts multiple actions on PC cell lines through its receptors subtypes 1A, 1B and 1D. It acts as a metogenic factor for tumoral cells. Prostate has 5- HT receptors and 5- HT releasing neuroendocrine (NE) cells. Prostatic tumour progression and poor prognosis was correlated with increase in number of 5- HT releasing NE cells on prostate and loss of androgen dependence. It was also seen that low doses of 5-HT can inhibit tumour growth via the decrease of blood supply to the tumour (4).

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CONFLICT OF INTEREST

None.

REFERENCES

1. Ross MH, Pawlina W. Male reproductive system. Histology: A Text and Atlas. 2016;790-833.
2. Abdul M, Logothetis CJ, Hoosein NM. Growth-inhibitory effects of serotonin uptake inhibitors on human prostate carcinoma cell lines. J Urol. 1995;154(1):247-50.
3. Aggarwal A, Jethani SL, Rohatgi RK, et al. Effects of fluoxetine on testis of albino rats–A histological assessment. IJSER. 2012;3(7):1-5.
4. Diceyi N. Expression of serotonin receptors and role of serotonin in human prostate cancer tissue and cell lines. Prostate. 2004;59(3):328-36.

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