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Impact of α-Adrenoceptor Antagonists on Biochemical Relapse in Men Undergoing Radiotherapy for Localised Prostate Cancer

Authors : Briohny H. Spencer, Russ Chess-Williams, Catherine McDermott, Shailendra Anoopkumar-Dukie, David Christie

Abstract : Background: Prostate cancer is the second most common cancer diagnosed in men worldwide and the most prevalent in Australian men. In 2015, it was estimated that approximately 18,000 new cases of prostate cancer were diagnosed in Australia. Currently, for localised disease, androgen depravation therapy (ADT) and radiotherapy are a major part of the curative management of prostate cancer. ADT acts to reduce the levels of circulating androgens, primarily testosterone and the locally produced androgen, dihydrotestosterone (DHT), or by preventing the subsequent activation of the androgen receptor. Thus, the growth of the cancerous cells can be reduced or ceased. Radiation techniques such as brachytherapy (radiation delivered directly to the prostate by transperineal implant) or external beam radiation therapy (exposure to a sufficient dose of radiation aimed at eradicating malignant cells) are also common techniques used in the treatment of this condition. Radiotherapy (RT) has significant limitations, including reduced effectiveness in treating malignant cells present in hypoxic microenvironments leading to radio-resistance and poor clinical outcomes and also the significant side effects for the patients. Alpha1-adrenoceptor antagonists are used for many prostate cancer patients to control lower urinary tract symptoms, due to the progression of the disease itself or may arise as an adverse effect of the radiotherapy treatment. In Australia, a significant number (not a majority) of patients receive a α1-ADR antagonist and four drugs are available including prazosin, terazosin, alfuzosin and tamsulosin. There is currently limited published data on the effects of α1-ADR antagonists during radiotherapy, but it suggests these medications may improve patient outcomes by enhancing the effect of radiotherapy. Aim: To determine the impact of α1-ADR antagonists treatments on time to biochemical relapse following radiotherapy. Methods: A retrospective study of male patients receiving radiotherapy for biopsy-proven localised prostate cancer was undertaken to compare cancer outcomes for drug-naïve patients and those receiving α1-ADR antagonist treatments. Ethical approval for the collection of data at Genesis CancerCare QLD was obtained and biochemical relapse (defined by a PSA rise of >2ng/mL above the nadir) was recorded in months. Rates of biochemical relapse, prostate specific antigen doubling time (PSADT) and Kaplan-Meier survival curves were also compared. Treatment groups were those receiving α1-ADR antagonists treatment before or concurrent with their radiotherapy. Data was statistically analysed using One-way ANOVA and results expressed as mean ± standard deviation. Major findings: The mean time to biochemical relapse for tamsulosin, prazosin, alfuzosin and controls were 45.3±17.4 (n=36), 41.5±19.6 (n=11), 29.3±6.02 (n=6) and 36.5±17.6 (n=16) months respectively. Tamsulosin, prazosin but not alfuzosin delayed time to biochemical relapse although the differences were not statistically significant. Conclusion: Preliminary data for the prior and/or concurrent use of tamsulosin and prazosin showed a positive trend in delaying time to biochemical relapse although no statistical significance was shown. Larger clinical studies are indicated and with thousands of patient records yet to be analysed, it may determine if there is a significant effect of these drugs on control of prostate cancer.

Keywords : alpha1-adrenoceptor antagonists, biochemical relapse, prostate cancer, radiotherapy
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