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ORIGINAL ARTICLE

Prostate cancer incidence in patients on 5α-reductase inhibitors for lower urinary tract symptoms: A 14-year retrospective study

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Summary There is still much debate regarding the long-term effect of 5α-reductase inhibitors (5-ARI) on the development of prostate cancer (PC). We tested the incidence of prostate cancer and the tumour Gleason grading in a non-screened population who were prescribed 5-ARIs for lower urinary tract symptoms (LUTS). Data from a prostatic biopsy database were analysed in a retrospective study, and included a period of 14 years (01/01/1997 to 01/01/2011). Those patients who were on 5-ARIs with either finasteride or dutasteride for less than 1 year were excluded. Patients who presented with LUTS and underwent diagnostic prostatic biopsies were included in this study. This patient cohort was further categorised according to their history of 5-ARIs medication.

The incidence of PC in the 5-ARI treated group was 15.4% ($n = 22/143$), comparable to that of the untreated group (16.7%, $n = 332/1990$) ($p = 0.7318$). Mean Gleason sum score and respective grade was the same ($7 = 3 + 4$) (median sum score 7 (range 6—10)). Average age at the time of PC diagnosis was similar regardless of 5-ARIs treatment: 72 (range 50—84) and 73 (45—84) years for treated and untreated groups, respectively.

In this retrospective study, patients treated with 5-ARIs for LUTS had similar risk in developing PC when compared to those who did not receive 5-ARIs. The Gleason sum scores for the cancers were similar in the two groups.

Abbreviations: 5-ARI, 5α-reductase inhibitors; LUTS, lower urinary tract symptoms; PC, prostate cancer; PCPT, prostate cancer prevention trial; PSA, prostate specific antigen; TRUS, transrectal ultrasound.

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Introduction

In 2003 the Prostate Cancer Prevention Trial (PCPT) demonstrated that in a screened population finasteride lowers the incidence of prostate cancer (PC), but the subsequent Gleason grades of the cancers were found to be higher [1]. This finding was further supported by a more recent report on the use of dutasteride [2,3]. Nonetheless, medical treatment with 5α-reductase inhibitors for symptomatic lower urinary tract symptoms (LUTS) remains widely used. It is worth noting that the 'Warnings and Precautions' section of the labels for the 5-alpha reductase inhibitor (5-ARI) class of drugs has been revised to include safety information about the increased risk of future diagnosis with a more serious form of prostate cancer (high-grade prostate cancer) [4] This risk appears to be low, and healthcare professionals are recommended to be aware of this safety information, and weigh the known benefits against the potential risks when deciding to start or continue treatment with 5-ARIs in men with symptomatic LUTS.

Given the difference between the highly motivated nature of patients participating in clinical trials and those who are routinely encountered in everyday practice within the National Health Service, we undertook a retrospective analysis of patients from a non-screened population presenting with lower urinary tract symptoms secondary to benign prostatic hyperplasia (BPH) and studied the incidence and tumour grade of prostate cancer identified within our patient cohort. By studying relevant patient cohorts with follow up information for up to 14 years, we tested if the reported risk of more aggressive prostate cancer was also present in our patients receiving 5-ARIs.

Patients and methods

We carried out a retrospective analysis of patients who attended our prostate assessment clinic over a 14-year period (01/01/1997 to 01/01/2011) at the Urology Unit, Southern General Hospital, NHS Greater Glasgow and Clyde. All data from this service are kept on a computerised audit system and comply with guidelines within our health board. We categorised our patient cohorts into two groups:

- Group 1 — Patients presenting with lower urinary tract symptoms who have been previously commenced on finasteride (5 mg once daily) or dutasteride (0.5 mg once daily) for at least 1 year.
- Group 2 (control) — Patients presenting with LUTS without previous medication of 5-ARIs.

Within the above two patient cohorts, we were able to identify individuals from each group who then subsequently underwent transrectal ultrasound (TRUS) scan guided prostatic biopsies; typically, at least 8 cores were obtained as per protocol. Prostatic biopsies were indicated either for an elevated PSA levels (>4 μg/mL; in 74%) or in the presence of abnormal digital rectal examination (DRE) (26%). The decision to biopsy was based on the absolute PSA levels and not the rate of PSA change (i.e. dynamics). A proportion of patients had both elevated PSA and abnormal DRE (18%). In our unit and consistent with recommended clinical practice, we compensate for the effects of 5-ARIs on serum PSA levels with a factor of two by multiplying individual PSA readings by 2 in men receiving treatment for over 12 months. Thus biopsies were taken in men on 5-ARIs if they had abnormal DREs and/or a PSA of >2 μg/mL (if they had been on treatment continuously for over 12 months). These abnormalities were identified either by the patients' general practitioners or during the patients' attendance at the prostate assessment clinic following their presentation with lower urinary tract symptoms. The following information were also collected in our study: patient age, urinary symptoms, pre-biopsy prostate specific antigen (PSA) and all subsequent pathology data such as Gleason grade. There were no age restrictions, but we excluded any patients with previous prostatic surgery. Our primary objective was to compare the incidence and Gleason score/grade of PC in both study groups.

Statistical analysis with Chi squared test was used to study the relationship of the incidence of PC and the respective tumour grades in the two patient groups. Analysis was performed using the Minitab v.15 (Minitab Inc., PA, USA).

Results

Analysis of our database showed that over the 14-year period (1997—2011), 10,446 patients were investigated for LUTS secondary to BPH, with 1146 (10.9%) of these patients on treatment with a 5-ARI (finasteride $n = 907$ (79.1%), dutasteride $n = 239$ (20.9%)). In 2133 (20.4%) patients, TRUS guided prostatic biopsies were carried out subsequently. Amongst these 2133 patients, a total of 143 patients were on a 5-ARI: 114 patients received medication with finasteride whilst 29 patients were prescribed dutasteride for at least twelve months. The median duration on finasteride was 3.3 years (range 1.1—8.9) and dutasteride was 2.8 years