Aspirin and levofloxacin for the prevention of the occurrence of prostate cancer or transformation to castration-resistant prostate cancer: a two-part, open-label, randomised, controlled study.


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Abstract

BACKGROUND: The role that inflammation plays in the development of prostate cancer is unknown. We aimed to assess whether an anti-inflammatory drug or antibiotic, or both, could prevent prostate cancer occurrence and delay transformation to castration-resistant prostate cancer.

METHODS: This open-label, randomised, controlled trial recruited participants who had undergone a prostate biopsy in West China Hospital of Sichuan University. Participants older than 40 years pathologically confirmed not to have prostate cancer but who had a prostate with inflammatory cell infiltration were assigned to the prostate cancer prevention (PCP) trial, and those older than 50 years who had pathological results of prostate cancer and were suitable for only androgen-deprivation therapy were assigned to the castration-resistant prostate cancer prevention (C-RPCP) trial. We excluded patients with haematological disease, gastrointestinal disease, and mental illness. Participants in both phases were randomly assigned (1:1:1:1) to a blank control group (no intervention), aspirin (100 mg/day until diagnosis or progression), levofloxacin (500 mg/day for 4 weeks), or aspirin plus levofloxacin. The coprimary outcomes were the number of newly diagnosed patients with prostate cancer and castration-resistant prostate cancer, and the durations from benign disease to malignancy and from androgen-dependent prostate cancer to castration-resistant prostate cancer, analysed by intention to treat. Patients were followed up for 2 years or until prostate cancer diagnosis or castration-resistant prostate cancer diagnosis. All participants provided written informed consent. The trial was approved by the hospital's clinical trials and biomedical ethics committee. This trial is registered with ClinicalTrials.gov, number NCT02757365.

FINDINGS: Between May 1, 2014, and April 30, 2016, we recruited 53 patients for the PCP trial (24 assigned to control, ten to aspirin, 12 to levofloxacin, and seven to aspirin plus levofloxacin) and 80 patients for the C-RPCP trial (17 assigned to control, 22 to aspirin, 23 to levofloxacin, and 18 to aspirin plus levofloxacin). Median follow-up time was 13·03 months (IQR 7·07-19·47...
for patients in the PCP trial and 18·17 months (11·40-22·34) for patients in the C-RPCP trial. In the PCP phase, none of the participants were pathologically proven to have prostate cancer at study end; therefore, the period from benign prostatic hyperplasia to prostate cancer did not differ between treatment groups (p=0·378). In the C-RPCP phase, the proportion of patients who developed castration-resistant prostate cancer did not significantly differ between groups (five [29%] with control, three [14%] with aspirin, three [13%] with levofloxacin, and three [17%] with aspirin plus levofloxacin; p=0·527). The median time from androgen-dependent prostate cancer to castration-resistant prostate cancer was 21·53 months (IQR 12·83-21·80) in the control group, 21·00 months (20·50-21·99) in the aspirin group, 16·53 months (14·68-17·00) in the levofloxacin group, and 25·00 months (21·02-25·00) in the aspirin plus levofloxacin group (p=0·222). In the C-RPCP phase, seven (41%) patients reported tumour-associated adverse events in the control group, compared with six (27%) with aspirin, five (22%) with levofloxacin, and eight (44%) with aspirin plus levofloxacin. Two (9%) patients on aspirin had drug-associated adverse effects compared with none in any of the other groups. No patients had serious complications and withdrew from the study because of adverse effects.

**INTERPRETATION:** Our data do not show that aspirin or levofloxacin help to decrease the incidence of prostate cancer occurrence, delay castration-resistant prostate cancer transformation, or reduce tumour-associated death. A longer period of follow-up and a larger number of patients are needed to draw final conclusions.

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