INTRODUCTION

Review question / Objective: After successful treatment with ADT, most patients with advanced disease eventually develop resistance and progress to castration-resistant PCa (CRPC), which remains an incurable disease. Low survival and high mortality of PCa are associated with the appearance of CRPC and subsequent metastatic disease. To advance the fight against PCa, it is necessary to continue basic and clinical research to improve testing, prevention and treatment practices. However, under current treatments, prevention should be seen as a basic strategy to reduce PCa morbidity and mortality. Epidemiological studies have shown that a healthy diet may significantly affect the occurrence and progression of prostate cancer. After promising preclinical testing, several natural compounds have been evaluated in the clinic. In this study, we compared data from clinical trials on several natural chemopreventive drugs as well as chemopreventive agents that have been tested for PCa chemoprevention. Provides some grounding support for preventing the progression of prostate cancer.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 August 2022 and was last updated on 10 August 2022 (registration number INPLASY202280037).
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Condition being studied: The WHO pointed out that the adoption of active prevention, early screening, standardized treatment and other measures has a significant effect on reducing the incidence and mortality of cancer. If the prostate cancer patient is not treated, the patient will have the progression and aggravation of the disease, especially the bone metastasis of prostate cancer cells, which will cause obvious pain in the patient, and even pathological fractures, which will seriously affect the quality of life of the patient and affect the survival time of the patient. For now, there is no cure for prostate cancer. Traditionally, the development and progression of PCa has been thought to be driven by androgens and androgen receptors (AR), hence the use of first-line therapy androgen deprivation therapy (ADT).

METHODS

Participant or population: Prostate cancer.

Intervention: The experimental group intervened in prostate cancer by taking different immunotrophic preparations daily.

Comparator: The control group took a placebo.

Study designs to be included: Clinical randomized controlled trials.

Eligibility criteria: (1) Studies with incomplete or unreported data (2) from non-randomised controlled trials [including quasi-randomised controlled trials, animal studies, protocols, conference summaries, case reports, or correspondence].

Information sources: Pubmede, Embas, Cochranelibrary and CNKI.

Main outcome(s): Changes in Serum total PSA.

Quality assessment / Risk of bias analysis: Two researchers independently assessed the risk of bias (ROB) of ROBs in RCT according to Cochrane Manual Version 5.1.0. Seven areas were considered: (1) random sequence generation, (2) treatment allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessments, (5) incomplete outcome data, (6) selective reporting and (7) other biases. The trial was divided into three ROB levels based on the number of ingredients that may have high ROB: high risk (5 or more), moderate risk (3 or 4), and low risk (2 or fewer). Reports publicly stored in existing databases should specify where the data would be stored and provide the relevant entry numbers. If you have not been given an accession number at the time of submission, please indicate that it will be provided during the review period. They must be provided prior to release. Interventional studies involving animals or humans, as well as other studies that require ethical approval, must list the authorities providing the approval and the corresponding code of ethical approval.

Strategy of data synthesis: In studies with immunotrophic agents as an intervention, all variables were continuous and expressed as means with standard deviation (SD). The continuous variables in the study will be reported as mean differences (MD = absolute difference between the two sets of means, defined as the mean difference between the treatment and control groups and calculated using the same scale) or standardized mean differences (SMD = mean difference
between outcomes between groups/standard deviation of outcomes between subjects, used to combine data when trials have different scales) and 95% confidence intervals (CI) and analysis. Since there are certainly potential differences between the different studies, we chose a random-effects model for analysis rather than a fixed-effects model. We use the Stata software (version 15.1) and use the Bayesian-based Markov Chain Monte Carlo Simulation Chain for NMA aggregation and analysis framework according to the PRISMA NMA Instruction Manual. We will use the node method to quantify and prove the consistency between indirect and direct comparisons, calculated by instructions in the Stata software, if the P-value > 0.05. The conformance test passes. Stata software is used to present and describe network diagrams of different immunotrophic interventions. In the generated network graph, each node represents a different immunotrophic agent intervention and different control conditions, and the lines connecting the nodes represent a direct head-to-head comparison between interventions. The size of each node and the width of the connecting lines are proportional to the number of studies. The level of intervention was summarized and reported as a P score. The P-score is thought to be a frequency simulation (SUCRA) that occurs under the cumulative ranking curve to assess and measure the degree of certainty that one treatment is superior to another, averaging across all competing treatments. The P-score ranges from 0 to 1, where 1 indicates optimal treatment with no uncertainty and 0 indicates worst treatment with no uncertainty. While P scores or SUCRA can be effectively represented as a percentage of the effectiveness or acceptability of exercise interventions, these scores should be interpreted with caution unless there are differences of practical clinical significance between interventions. To check for the presence of bias due to small-scale studies, which can lead to publication bias in the NMA, a network funnel diagram is generated and visual inspection is performed using symmetry criteria.

**Subgroup analysis:** Not carried out.

**Sensitivity analysis:** Not carried out.

**Country(ies) involved:** China.

**Keywords:** prostate cancer Prostate-specific antigen Immunotrophic preparations chemoprophylaxis.

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