

Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer.

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PURPOSE: Phytochemicals in plants may have cancer preventive benefits through antioxidation and via gene-nutrient interactions. We sought to determine the effects of pomegranate juice (a major source of antioxidants) consumption on prostate-specific antigen (PSA) progression in men with a rising PSA following primary therapy. **EXPERIMENTAL DESIGN:** A phase II, Simon two-stage clinical trial for men with rising PSA after surgery or radiotherapy was conducted. Eligible patients had a detectable PSA > 0.2 and < 5 ng/mL and Gleason score < or = 7. Patients were treated with 8 ounces of pomegranate juice daily (Wonderful variety, 570 mg total polyphenol gallic acid equivalents) until disease progression. Clinical end points included safety and effect on serum PSA, serum-induced proliferation and apoptosis of LNCaP cells, serum lipid peroxidation, and serum nitric oxide levels. **RESULTS:** The study was fully accrued after efficacy criteria were met. There were no serious adverse events reported and the treatment was well tolerated. Mean PSA doubling time significantly increased with treatment from a mean of 15 months at baseline to 54 months posttreatment ($P < 0.001$). In vitro assays comparing pretreatment and posttreatment patient serum on the growth of LNCaP showed a 12% decrease in cell proliferation and a 17% increase in apoptosis ($P = 0.0048$ and 0.0004 , respectively), a 23% increase in serum nitric oxide ($P = 0.0085$), and significant ($P < 0.02$) reductions in oxidative state and sensitivity to oxidation of serum lipids after versus before pomegranate juice consumption. **CONCLUSIONS:** We report the first clinical trial of pomegranate juice in patients with prostate cancer. The statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer in vitro cell proliferation and apoptosis as well as oxidative stress, warrant further testing in a placebo-controlled study.