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Six Weeks of Fluoroquinolone Antibiotic Therapy for Patients with Elevated Serum PSA is not Clinically Beneficial: A Randomized Controlled Clinical Trial (#URL-D-15-01365R2)

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Prostate specific antigen (PSA) levels are often evaluated in an attempt to detect early prostate cancer, however false positive PSA tests are common.¹ A strategy to limit false positives, surrounding concerns that prostatitis may increase PSA, has been to defer biopsy decisions until after a course of antibiotics and repeat PSA measurement. This strategy has been evaluated in prior studies, including several small randomized trials, with differing conclusions regarding its benefit.^{2–4}

The authors report a prospective, randomized trial investigating the impact of six weeks of fluoroquinolone antibiotics on PSA levels in asymptomatic men with an elevated PSA. This single-institution study randomized 150 of 1,151 eligible patients with a PSA between 4.0 and 20.0 ng/mL to 6 weeks of fluoroquinolone therapy (ciprofloxacin, but due to formulary changes a proportion received levofloxacin) or 6 weeks of observation. The primary endpoint was change in PSA 8 weeks after randomization. Rate of cancer diagnosis was a secondary outcome for patients who received a biopsy. A near significant difference in the change in PSA across groups was reported (–0.68 vs. 0.01 ng/mL for treatment and observation groups, respectively, $p=0.052$). 62% of treatment patients and 72% of observation patients underwent biopsy with no difference in cancer detection rate (63% vs. 52%, respectively, $p=0.60$). The authors conclude that asymptomatic patients with elevated PSA should not receive antibiotics prior to determining if a prostate biopsy is warranted.

While the authors are commended for completing a prospective randomized trial to inform the debate on this urological practice, one limitation of this study is the lack of a pre-trial power calculation to plan enrollment. Despite this limitation, the post-intervention median PSA levels in both the treatment and observation groups were above most accepted biopsy thresholds (5.1 ng/mL and 5.0 ng/mL, respectively), indicating that even if the study had found a statistically significant difference, it may not have been clinically relevant. Also, as shown in this study, a decrease in PSA does not indicate an absence of prostate cancer.

Given this trial and others on the topic have not provided convincing evidence of this practice, the authors are correct in concluding evidence does not support this management strategy. The risks and costs associated with unnecessary antibiotics are not trivial.⁵ When hospitalizations after transrectal prostate biopsy were assessed in the Michigan Urological Surgery Improvement Collaborative (MUSIC), 95% of hospital admissions were for infectious complications, and the majority of cultures identified fluoroquinolone resistant

organisms.⁶ With rising antibiotic resistance⁷ and in an era increasingly focused on quality care and appropriate healthcare utilization, we do not recommend antibiotic therapy prior to making decisions about prostate biopsy in asymptomatic men with elevated PSA. This practice is also highlighted within the American Board of Internal Medicine and American Urological Association's Choosing Wisely campaign as something that physicians and patients should question.⁸

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