POEMs

Preexposure Prophylaxis with Tenofovir/Emtricitabine Prevents HIV Infection in Men Who Have Unprotected Anal Intercourse

Clinical Question

Among men who have unprotected anal intercourse, does the combination of tenofovir/emtricitabine (Truvada) taken before and after intercourse reduce the risk of human immunodeficiency virus (HIV) infection?

Bottom Line

Preexposure prophylaxis in high-risk men who have unprotected anal intercourse reduces the likelihood of developing HIV (number needed to treat = 17 per year). Participants averaged 15 pills per month, which costs approximately $700 per month ($8,400 per year). Condoms would be a much more cost-effective way to prevent HIV infection (although condoms were not compared with medications in this study). (Level of Evidence = 1b)

Synopsis

The researchers identified 400 HIV-negative men who had unprotected anal intercourse with at least two men in the previous six months. Those with impaired renal function, hepatitis B virus infection, or hepatitis C virus infection were excluded. The patients were randomized to receive tenofovir/emtricitabine, 300 mg/200 mg, or matching placebo. They were told to take two pills between two and 24 hours before intercourse, and a third and fourth pill at 24 and 48 hours after the first two pills were taken. The median age of participants was 35 years, 92% were white, and 73% were not currently in a relationship. The groups were balanced at the beginning of the study, and analysis was by intention to treat. Patients had regular clinic visits and were followed for a median of 9.3 months. Follow-up was good, with a similar number lost in each group (23 and 26 patients). Adherence was also good, with more than 80% having serologic evidence of having taken the drugs in the previous week. Patients in the intervention group were less likely to develop HIV during the study period than those in the placebo group (2 vs. 14 infections, or 0.91 vs. 6.6 per 100 person-years of follow-up; $P = .002$, number needed to treat = 17 per year). Gastrointestinal adverse effects were more common in the intervention group (14% vs. 5%; $P = .002$), but otherwise the medication was safe and well tolerated.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Population-based

Reference: *Molina JM, Capitant C, Spire B, et al.; ANRS IPERGAY Study Group. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection.* N Engl J Med. *2015;373(23):2237-2246.*

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Systolic BP of 120 Instead of 140 in High-Risk Older Patients Without Diabetes Leads to Significant Benefits and Some Harms

Clinical Question

Is there a net benefit to a systolic blood pressure (BP) target of 120 mm Hg compared with 140 mm Hg in patients without diabetes mellitus who are at high risk of cardiovascular disease?

Bottom Line

In this group of older patients (mean age = 68 years) who do not have diabetes but are at high risk of cardiovascular disease, a more aggressive systolic BP target of 120 mm Hg instead of 140 mm Hg led to benefits (lower all-cause mortality, lower cardiovascular mortality, less heart failure), but also some harms (more serious episodes of hypotension, electrolyte abnormality, syncope, and acute kidney injury). Patients in the intensive therapy group ▶

took an average of one additional drug to achieve this target. The decision to pursue this more aggressive target should be guided by how well the patient fits the profile of patients in this study (i.e., no diabetes, older than 50 years, high risk of cardiovascular disease) and how well the additional therapy is tolerated. (Level of Evidence = 1b)

Synopsis

Previous trials of more aggressive BP targets in high-risk patients have shown no benefit or, in some cases, a benefit limited to only one of many possible clinical outcomes (e.g., hemorrhagic stroke only). This study identified patients 50 years and older with a baseline systolic BP between 130 and 180 mm Hg and no history of diabetes or stroke. All were at increased risk of cardiovascular complications based on at least one of the following: cardiovascular disease, chronic kidney disease (glomerular filtration rate [GFR] = 20 to 60 mL per minute), 10-year cardiovascular risk of 15% or more based on the Framingham risk score, or at least 75 years of age. Only outcome assessors were masked to the treatment assignment; patients and their physicians were not. Details regarding allocation concealment were not provided, but the groups were balanced with regard to demographics, baseline BP, and cardiovascular risk factors. Of 14,692 patients screened for eligibility, 9,361 were randomized to a systolic BP target of 120 or 140 mm Hg. The mean age of participants was 68 years, 56% were current or former smokers, 30% were non-Hispanic black, and 11% were Hispanic. The most common reasons for exclusion before randomization were lack of cardiovascular risk, out-of-range systolic BP, or the use of too many BP medications.

The protocol for the 120 mm Hg group specified beginning with two- or three-drug therapy with a combination of a thiazide diuretic, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and/or a calcium channel blocker; those in the 140 mm Hg group were converted from their usual drug to an equivalent in the formulary. The formulary included a broad range of medications, including most of the drugs most commonly prescribed in the United States. The exception was that hydrochlorothiazide was available only in combination with triamterene (Dyazide) at a dose of 50 mg; chlorthalidone, furosemide (Lasix), spironolactone, and amiloride (Midamor) were the other diuretics. Drugs were added from the formulary as needed to achieve BP targets. The average number of agents used in the 120 mm Hg group was 2.7, with 32% of patients requiring three drugs and 24% of patients requiring four or more drugs. In the 140 mm Hg group, the average number of medications was 1.8, and only 17% of patients required three drugs and 7% required four or more. Clinical outcomes and adverse events were adjudicated by a committee masked to treatment assignment. Analysis was by intention to treat, and the mean BPs achieved in the two groups were 121 and 136 mm Hg.

Although the study originally planned a five-year follow-up, it was halted after 3.3 years on the basis of positive findings in an interim analysis. The intensive treatment group was less likely to die from any cause (3.3% vs. 4.5%; $P = .003$; number needed to treat [NNT] = 83 over 3.3 years), less likely to die from a cardiovascular cause (0.8% vs. 1.4%; $P = .005$; NNT = 167 over 3.3 years), and less likely to develop heart failure (1.3% vs. 2.1%; $P = .002$; NNT = 125 over 3.3 years). There were no significant differences in the likelihood of myocardial infarction, acute coronary syndrome, or stroke. Among the patients with chronic kidney disease at baseline (n = 2,646), there was no difference in the likelihood of end-stage renal disease or a 50% or higher reduction in GFR. Among those without chronic kidney disease, there was a small increase in the likelihood of a 30% or greater decline in GFR (3.8% vs. 1.1%; $P = .001$; NNT = 37 over 3.3 years). The benefits became apparent after two to three years of therapy based on the Kaplan-Meier curves. Looking at a composite outcome of myocardial infarction, acute coronary syndrome, stroke, heart failure, or cardiovascular death, benefits appeared to be somewhat greater among patients older than 75 years and for men.

Although there were clear benefits, there were also harms. Serious adverse events were defined as fatal or life-threatening, resulting in disability, or requiring hospitalization. Episodes of hypotension (2.4% vs. 1.4%), syncope (2.3% vs. 1.7%), electrolyte abnormality (3.1% vs. 2.3%), and acute kidney injury or acute renal failure (4.1% vs. 2.5%) were all significantly more common in the intensive therapy group.

Study design: Randomized controlled trial (single-blinded)

Funding source: Government

Allocation: Uncertain

Setting: Outpatient (any)

Reference: *Wright JT Jr, Williamson JD, Whelton PK, et al.; SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control.* N Engl J Med. *2015;373(22):2103-2116.*

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