

Though often prescribed, diuretic pills may not prevent kidney stones

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A new study is raising questions about the effectiveness of medications



long used to prevent painful kidney stones, but experts say there's no reason for patients to toss their prescriptions out at this point.

Anyone who has ever passed a <u>kidney stone</u> would prefer to avoid a repeat experience. And for many years, doctors have prescribed thiazide diuretics as one preventive tactic.

Based on studies done decades ago, the cheap medications became a cornerstone of thwarting recurrences in people who have calcium-based kidney stones (as most stones are).

But a new clinical trial, published March 2 in the *New England Journal* of *Medicine*, has come to a surprising conclusion: Thiazide diuretics may work no better than a placebo.

Swiss researchers found that over three years, <u>patients</u> randomly assigned to a daily diuretic dose had similar rates of <u>kidney</u> stone recurrence as patients given a placebo. Anywhere from 49% to 59% developed kidney stone symptoms or showed X-ray evidence of a new stone or growth in an old stone.

The lowest rate of recurrence—49%—was seen in patients on the highest diuretic dose. But statistically speaking, their risk was not significantly different from the placebo group's recurrence rate.

The results are sure to surprise doctors who treat kidney stones for a living, said <u>Dr. Todd Alexander</u>, a professor of pediatrics and pediatric nephrology at the University of Alberta, in Edmonton, Canada.

But Alexander, who wrote an <u>editorial</u> published with the study, felt the findings are still not enough to change standard care.

"Do I think we should throw away these medications we've been using



for 50 years, based on <u>clinical trials</u> and our clinical experience?" he said. "No."

Alexander pointed to what he sees as a central limitation of the trial: the relatively small numbers of participants.

The researchers, led by <u>Dr. Daniel Fuster</u> of Bern University Hospital, recruited 416 patients and randomly assigned them to four different groups: three were given different doses of a diuretic called hydrochlorothiazide, while one group was given an inactive placebo.

That amounted to about 100 patients in each group, Alexander said, which may not have been enough to detect differences among them.

<u>Dr. Mantu Gupta</u>, director of endourology and stone disease at the Mount Sinai Health System in New York City, had a blunt take on the findings.

"This is a very well-conducted trial, but horribly conceived," Gupta said.

That's because it veers from common real-world practice, according to Gupta. For one, he said, thiazide diuretics are not prescribed to everyone with kidney stones, only to certain patients most likely to benefit.

That means people who have calcium stones and high levels of calcium in their urine: Thiazide diuretics are thought to cut the risk of kidney stones because they reduce calcium excretion into the urine.

The trial included patients who had high urinary calcium levels, but more than one-third did not.

Gupta also said the specific diuretic regimen was problematic: Hydrochlorothiazide is short-acting, he noted, and patients took it once a



day. Instead, Gupta said, a longer-acting diuretic would normally be used, or if hydrochlorothiazide were prescribed, it would be taken twice daily.

Given the trial limitations, both doctors said they would not be changing their practice.

Alexander, a pediatric kidney specialist, regularly uses thiazide diuretics to help prevent stones in kids.

"This is one study," he said. "It's not going to change what I do."

Kidney stones are common, affecting about 10% of people at some point, according to the National Kidney Foundation. Often, they can be passed in the urine. But if a large stone causes a urine blockage or too much agony, doctors may need to remove it.

To help prevent a recurrence, people can try diet changes, like getting plenty of fluids, fruits and vegetables. For people with high urinary calcium, it's important to limit sodium—including when they're on a thiazide diuretic, Gupta said, because the medications work best when urine sodium is low.

For patients who have been using diuretics to prevent kidney stones, there is no reason to stop, both doctors said.

"This doesn't mean you're on the wrong medication," Gupta said.

But, he added, people prone to stones should always discuss the <u>treatment options</u> with their doctor, and whether a thiazide diuretic is, in fact, right for them.

Alexander made another point: Even if diuretics reduce stone



recurrences, they clearly do not eliminate them. And the medications can have side effects, like lowered potassium levels and effects on <u>blood</u> <u>sugar</u> that may precipitate diabetes in some people.

This trial, Alexander said, highlights that bigger picture. "We do need better therapies," he said.

More information: The American Urological Association has more on managing <u>kidney stones</u>.

Nasser A. Dhayat et al, Hydrochlorothiazide and Prevention of Kidney-Stone Recurrence, *New England Journal of Medicine* (2023). <u>DOI:</u> 10.1056/NEJMoa2209275

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