

Antibiotic, Spironolactone Combo Ups Sudden Death in Elderly

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Prescribing the widely used antibiotic trimethoprim-sulfamethoxazole in tandem with spironolactone, a diuretic used to treat patients with heart failure, can double an older patient's risk for sudden death, according to results from a Canadian study. The study was [published online](#) February 2 in the *Canadian Medical Association Journal*.

Researchers led by Tony Antoniou, PhD, from St. Michael's Hospital in Toronto, Ontario, Canada, examined data from patients aged 66 years or older who were treated with spironolactone between 1994 and 2011. Data analyzed came from patients' prescription, hospital admission, and health insurance records, as well as basic demographic data from the province of Ontario's Office of the Registrar General. Of the group of 206,319 patients studied, 11,968 died suddenly and 349 died within 14 days of being prescribed one of five antibiotics.

Overall, 29,141 courses of trimethoprim-sulfamethoxazole in patients prescribed spironolactone were linked to 215 deaths within 14 days, for a rate of 0.74%.

Patients who were prescribed trimethoprim-sulfamethoxazole had more than twice (adjusted odds ratio [OR], 2.46; 95% confidence interval [CI], 1.55 - 3.90) the risk for sudden death compared with patients who were prescribed amoxicillin, another common antibiotic.

Of the other antibiotics in the study, ciprofloxacin (adjusted OR, 1.55; 95% CI, 1.02 - 2.38) and nitrofurantoin (adjusted OR, 1.70; 95% CI, 1.03 - 2.79) also showed an increased risk compared with amoxicillin, although the risk diminished in nitrofurantoin on further analysis. Norfloxacin (adjusted OR, 0.86; 95% CI, 0.47 - 1.58) showed no such risk.

More than 20 million trimethoprim prescriptions are written in the United States each year. The drug is most often used in treating urinary tract infections in combination with the drug sulfamethoxazole.

The authors note that "[t]rimethoprim-sulfamethoxazole and spironolactone are commonly prescribed medications, and the likelihood of co-prescription is high." They also note that physicians might overlook their dangers in patients with heart disease, mistakenly attributing deaths to heart disease, rather than hyperkalemia (a potentially fatal decrease in potassium).

Claudene George, MD, RPh, assistant professor of clinical medicine, geriatrics, at Albert Einstein College of Medicine, Bronx, New York, told *Medscape Medical News* that the study results were alarming and that they would change her prescribing practices.

"I will be more thoughtful when considering antibiotic options for patients on spironolactone," she said. "If suitable options do not exist, then potassium and kidney function should be closely followed during treatment."

Dr George said penicillin and cephalosporin may be suitable antibiotic alternatives. Ciprofloxacin is typically a good alternative "but was also associated with a significant risk of sudden cardiac death, which was surprising," she said.

If no suitable alternative exists, "physicians should monitor potassium and consider the patient's creatinine clearance when these drugs are used concomitantly."

Dr George added that she thought it was likely that kidney function plays a significant role in causing hyperkalemia and sudden death, something that was not explored in the study.

In a previous study, Dr Antoniou and colleagues found that trimethoprim-sulfamethoxazole, combined with spironolactone, was more than 12 times likelier than amoxicillin to cause hyperkalemia.

"We found that trimethoprim-sulfamethoxazole was associated with a marked increase in the risk of sudden death among older patients receiving spironolactone, a finding that we speculate reflects trimethoprim-induced hyperkalemia. We also found a less pronounced but clinically important association with ciprofloxacin, and possibly nitrofurantoin," the authors conclude. "When clinically appropriate, clinicians should consider alternative antibiotics for patients receiving spironolactone."

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