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ORIGINAL ARTICLE

Azithromycin and the Risk of Cardiovascular Death

Wayne A. Ray, Ph.D., Katherine T. Murray, M.D., Kathi Hall, B.S., Patrick G. Arbogast, Ph.D., and C. Michael Stein, M.B., Ch.B.

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BACKGROUND

Although several macrolide antibiotics are proarrhythmic and associated with an increased risk of sudden cardiac death, azithromycin is thought to have minimal cardiotoxicity. However, published reports of arrhythmias suggest that azithromycin may increase the risk of cardiovascular death.

METHODS

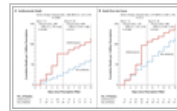
We studied a Tennessee Medicaid cohort designed to detect an increased risk of death related to short-term cardiac effects of medication, excluding patients with serious noncardiovascular illness and person-time during and shortly after hospitalization. The cohort included patients who took azithromycin (347,795 prescriptions), propensity-score–matched persons who took no antibiotics (1,391,180 control periods), and patients who took amoxicillin (1,348,672 prescriptions), ciprofloxacin (264,626 prescriptions), or levofloxacin (193,906 prescriptions).

RESULTS

During 5 days of therapy, patients taking azithromycin, as compared with those who took no antibiotics, had an increased risk of cardiovascular death (hazard ratio, 2.88; 95% confidence interval [CI], 1.79 to 4.63; $P < 0.001$) and death from any cause (hazard ratio, 1.85; 95% CI, 1.25 to 2.75; $P = 0.002$). Patients who took amoxicillin had no increase in the risk of death during this period. Relative to amoxicillin, azithromycin was associated with an increased risk of cardiovascular death (hazard ratio, 2.49; 95% CI, 1.38 to 4.50; $P = 0.002$) and death from any cause (hazard ratio, 2.02; 95% CI, 1.24 to 3.30; $P = 0.005$), with an estimated 47 additional cardiovascular deaths per 1 million courses; patients in the highest decile of risk for cardiovascular disease had an estimated 245 additional cardiovascular deaths per 1 million courses. The risk of cardiovascular death was significantly greater with azithromycin than with ciprofloxacin but did not differ significantly from that with levofloxacin.

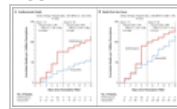
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FIGURE 1



Cumulative Incidence of Cardiovascular Death and Death from Any Cause among Patients Who Took Azithromycin and Persons Who Did Not Take Study Antibiotics during a 10-Day Period.

FIGURE 2



Cumulative Incidence of Cardiovascular Death and Death from Any Cause for Patients Who Took Azithromycin or Amoxicillin during a 10-Day Period.

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CONCLUSIONS

During 5 days of azithromycin therapy, there was a small absolute increase in cardiovascular deaths, which was most pronounced among patients with a high baseline risk of cardiovascular disease. (Funded by the National Heart, Lung, and Blood Institute and the Agency for Healthcare Quality and Research Centers for Education and Research on Therapeutics.)

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[Disclosure forms](#) provided by the authors are available with the full text of this article at NEJM.org.

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SOURCE INFORMATION

From the Division of Pharmacoepidemiology, Department of Preventive Medicine (W.A.R., K.H.), the Departments of Medicine and Pharmacology, Divisions of Cardiology (K.T.M.), Rheumatology (C.M.S.), and Clinical Pharmacology (K.T.M., C.M.S.), and the Department of Biostatistics (P.G.A.), Vanderbilt University School of Medicine; and the Geriatric Research Education and Clinical Center, Nashville Veterans Affairs Medical Center (W.A.R.) — both in Nashville.

Address reprint requests to Dr. Ray at the Department of Preventive Medicine, Village at Vanderbilt, Suite 2600, 1501 21st Ave. S., Nashville, TN 37212, or cindy.naron@vanderbilt.edu.

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