

Study Links Popular Antibiotic to Increased Risk of Sudden Death

ERYTHROMYCIN/DRUG COMBINATION MAY CAUSE FATAL HEART CONDITION

Editorial Staff

First launched under the brand name Ilosone, erythromycin was hailed as one of the "wonder drugs" produced by the pharmaceutical industry in the second half of the 20th century. Since its introduction in 1952, erythromycin has become one of the most popular antibiotics on the market, particularly because it can be administered to most people who are allergic to penicillin. It is available as a tablet, ointment, gel, oral suspension or injection, and has been prescribed by doctors to treat dozens of infectious diseases, ranging from syphilis and pneumonia to tonsillitis and strep throat.

Along with the benefits of erythromycin, however, come some potentially serious side-effects. In fact, previous research has suggested that high doses of erythromycin can cause adverse effects ranging from abdominal pain and diarrhea to an irregular heartbeat. Other studies have linked the use of erythromycin in combination with certain medications called CYP3A inhibitors to a life-threatening heart disorder called *torsades de pointes*, but the exact cause and importance of this relationship has remained unclear.

In a study published in the Sept. 9 issue of *The New England Journal of Medicine*, a team of American researchers found that taking erythromycin in conjunction with certain CYP3A inhibitors could increase the risk of sudden cardiac death by more than five times compared to people taking a CYP3A inhibitor by itself. The study also found that the risk of sudden cardiac death was twice as high among people taking erythromycin alone compared to people not taking other antibiotics.

In the study, researchers reviewed the medical records of 1,476 Medicaid recipients in Tennessee who had died suddenly from a cardiac-related condition between 1988 and 1993. The scientists looked for any association between erythromycin use and sudden cardiac death, and whether the risk was affected by concurrent use of six different CYP3A inhibitors (ketoconazole, itraconazole, fluconazole, diltiazem, verapamil, and troleandomycin), all of which are known to slow down the body's ability to metabolize certain drugs. When taken with erythromycin, they can cause elevated levels of the antibiotic to remain in the bloodstream for prolonged amounts of time.

In addition to current erythromycin use, the researchers examined the risk of sudden cardiac death in those who previously used erythromycin. They also studied the risk for people taking another antibiotic, amoxicillin, which is used to treat many of the same types of infections. Factors such as age, sex, race and type of Medicaid enrollment were included to provide as objective an assessment as possible.

The analysis showed that when patients used erythromycin concurrently with one of the CYP3A inhibitors, there was "a marked increase in the risk of sudden death from cardiac causes" - 5.35 times as high as patients who used neither CYP3A inhibitors nor any of the study antibiotics. There was no increase in risk among those who concurrently used amoxicillin and a CYP3A inhibitor, or those currently using any of the study antibiotics who had formerly used CYP3As.

The study also showed that patients who were currently taking erythromycin had a sudden cardiac death risk twice as high as patients who were former users of erythromycin; who were taking only amoxicillin; or who had never used either antibiotic.

To confirm their results, the researchers conducted several supplemental analyses to determine whether the increase in sudden cardiac death associated with erythromycin may have been the result of using other medications also known to cause an irregular heartbeat. They found that "the association between erythromycin and the risk of sudden death from cardiac causes was unchanged in all of these analysis."

Although they were unable to find the exact mechanism that leads to sudden cardiac death, the authors speculated that an increased concentration of erythromycin in the blood alters a person's heart rhythm by prolonging a portion of the heartbeat called the QT interval. Prolonging the QT interval is known to be associated with an increase in potentially fatal heart rhythms. "However, other factors may be involved," they added.

Although the study suffered from some limitations, such as a failure to include behavioral and lifestyle factors, the scientists were sufficiently convinced to conclude that erythromycin and CYP3A inhibitors should no longer be used together:

"In conclusion, patients who used both erythromycin and the study CYP3A inhibitors had a risk of sudden death from cardiac causes that was five times as great as that among patients who had not used these drugs. Given that there are alternatives to erythromycin and to most CYP3A inhibitors, the use of this combination should be avoided in clinical practice."

Practitioners Urge Caution, More Research

In an interview with the Associated Press, Dr. Wayne Ray, the study's lead author, said that more research needs to be done on the potential interactions between old medications such as erythromycin, and newer medications. "This is an unacceptably high risk," he said, adding, "There are other antibiotics that provide the same antimicrobial activity without building up in the blood the way erythromycin does."

Dr. Muhamed Saric, a cardiologist and director of the electrocardiology laboratory at the University of Medicine and Dentistry of New Jersey, stated that nobody realized the potential magnitude of the problem before the *NEJM* study was published, because most previous studies had analyzed deaths in patients given erythromycin intravenously. However, Ray's study focused on erythromycin pills, which are administered much more frequently than injections.

"It was thought that erythromycin is a generally safe drug," Dr. Saric said. He cautioned that family doctors are probably less likely to know about the potential interactions between erythromycin and other drugs than other health care providers.

"People may be taking these medications for years, and they develop a throat infection and someone gives them erythromycin, and that's it," Saric said.

In addition to the implications the *NEJM* study may have on the ongoing use of erythromycin, the results reveal several important issues that doctors of chiropractic should discuss with their patients. As a DC, ask your patients about all of the medications and over-the-counter supplements they may be taking. If a patient is on medication, make sure that it is absolutely necessary, and that all alternatives to the medication have been explored thoroughly. Medications should not be taken for unnecessary lengths of time; adding new drugs to an existing regimen should also be avoided if possible. And if a patient is prescribed a new medication, make sure the patient discusses it with

his or her doctor before beginning use.

References

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