Common antibiotic linked with heart deaths

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The antibiotic clarithromycin—widely used for treating common bacterial infections—is associated with an increased risk of heart deaths, finds a study published in the *BMJ* today.

The authors say their findings require urgent confirmation, given that many millions of people are prescribed the drug each year. But they stress that the absolute risk is small and that prescribing practice should not be changed until results have been confirmed in an independent study.

Clarithromycin belongs to a group of antibiotics known as macrolides. Macrolide antibiotics prolong the duration of electrical activity of the heart muscle (known as the QT interval) and are therefore thought to

increase the risk of potentially fatal heart rhythm problems.

Given this background, the cardiac safety profiles of individual macrolides need to be studied in greater detail to help guide clinical treatment decisions.

So a team of Danish researchers decided to assess the risk of cardiac death associated with clarithromycin and another macrolide called roxithromycin, compared with penicillin V, an antibiotic with no known cardiac risk.

Using national databases, they identified over 5 million treatment courses among Danish adults aged 40-74 years from 1997 to 2011 (160,297 with clarithromycin, 588,988 with roxithromycin and 4,355,309 with penicillin V).

Individuals with serious disease, who may be at high baseline risk of death, were excluded from the analysis.

A total of 285 cardiac deaths were observed during ongoing use with the study drugs, 18 of which occurred during use of clarithromycin and 32 during use of roxithromycin.

After adjusting for factors such as age, sex, baseline cardiac risk and use of other medication, ongoing use of clarithromycin was associated with a 76% higher risk of cardiac death compared with use of penicillin V. There was no increased risk of cardiac death with clarithromycin after treatment had ended.

The absolute risk difference was 37 cardiac deaths per 1 million courses with clarithromycin. No increased risk of cardiac death was found with ongoing or past use of roxithromycin.

"Our study expands on the available knowledge of the cardiac safety of macrolides, being the first large scale population based observational study to show significantly increased cardiac risk with clarithromycin and the relative cardiac safety of roxithromycin," write the authors.

The authors emphasise that the absolute increase in risk is small and should have limited, if any, effect on the prescribing practice in individual patients. However, they note, "clarithromycin is one of the more commonly used antibiotics in many countries and many millions of people are prescribed this drug each year; thus, the total number of excess (potentially avoidable) cardiac deaths may not be negligible."

Before these results are used to guide clinical decision making, "confirmation in independent populations is an urgent priority given the widespread use of macrolide antibiotics," they conclude.

More information: *BMJ*, www.bmj.com/cgi/doi/10.1136/bmj.g4930

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