

## Fatal Combination of Antibiotic and Calcium Channel Blocker Agents

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According to the new researches, clarithromycin prescribed for patients already taking antihypertensive calcium-channel blockers is associated with increased number of hospitalizations due to acute kidney injuries, hypotension, and death (1, 2). Clarithromycin is a cytochrome P450A4 inhibitor, which metabolizes calcium-channel blockers. Previous researches showed that the antibiotic can surge the blood calcium-channel blockers level to 500% of its normal level (1, 2). Gandhi et al. (3), from the London Health Sciences Centre and the University of Western Ontario, suggested that potentially hundreds of hospitalizations and deaths in our region may be associated with this largely preventable drug-drug interaction. This burden on the healthcare system, causing high costs on managing acute kidney injuries, might have been avoided (3).

A warning from the US Food and Drug Administration (4) states that "serious adverse reactions have been reported in patients taking clarithromycin concomitantly with CYP3A4 substrates, including hypotension with calcium-channel blockers metabolized by CYP3A4 (such as verapamil, amlodipine and diltiazem). The reasons for the continued use of the drugs, despite these warnings, still remain unclear (3). Since azithromycin is only a weak CYP3A4 inhibitor, the type of intensification of the calcium-channel blocker that occurs with clarithromycin is not estimated. The most common calcium-channel blocker - amlodipine - was prescribed for more than 50% of patients. In patients who take a calcium-channel blocker, the absolute risk of hospitalization for acute kidney injuries was higher, moreover, in patients taking clarithromycin this risk is greater than those taking azithromycin (0.44% vs. 0.22%; odds ratio [OR], 1.98). Patients taking clarithromycin also had a higher risk of hospitalization due to hypotension (OR, 1.60) and all-cause mortality rate (OR, 1.74). A subgroup analysis showed that dihydro-

pyridines, particularly nifedipine, as the calcium-channel blockers, are associated with the highest risk acute kidney injury (OR, 5.33), with an absolute risk increase of 0.63%. The risk with nifedipine was followed by felodipine and amlodipine (3).

The researchers previously confirmed that there are no significant differences between clarithromycin and azithromycin regarding the rates of 30-day hospitalization rate of patients with acute kidney injuries, in the absence of other interacting medications. The use of calcium-channel blockers alone, 90 days prior to the antibiotic administration, did not affect the 30-day outcomes (3). Due to the role of kidneys in eliminating clarithromycin, the guidelines called to reduce the antibiotic dose for patients with chronic kidney disease, but the researches showed that this rarely occurs in routine practices (3). "Clarithromycin may be the top choice antibiotic in some cases, particularly in severely immunosuppressed patients, such as patients with AIDS, or in the treatment of extremely drug-resistant microbe, but in these cases, it is perfectly feasible to take the patient off the calcium-channel blockers. Drug-drug interactions are usually under-recognized by doctors, but newer electronic prescribing programs with specific interaction recognition software will significantly decrease this risk (5).

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