

Gatifloxacin Induces Dysglycemia in Older Patients

Park-Wyllie LY, Juurlink DN, Kopp A, et al. Outpatient gatifloxacin therapy and dysglycemia in older adults. *N Engl J Med* 2006;354:1352–61.

Study Overview

Objective. To examine dysglycemia-related health outcomes associated with various antibiotics.

Design. 2 nested case-control studies.

Setting and participants. Case patients from both studies were identified from a cohort of approximately 1.4 million residents of Ontario, Canada, aged ≥ 66 years whose health care records indicated outpatient treatment with a broad-spectrum antibiotic. Patients were included if they were treated in the hospital for hypoglycemia (study 1) or hyperglycemia, diabetic ketoacidosis, or hyperosmolar non-ketotic coma (study 2) and had received outpatient therapy with a macrolide, an oral second-generation cephalosporin, or a respiratory fluoroquinolone (ie, gatifloxacin, levofloxacin, moxifloxacin, or ciprofloxacin) 30 days prior to presentation. For each case patient, 5 controls were identified and matched according to age, sex, the presence or absence of diabetes, and the timing of antibiotic therapy.

Main outcome measure. The association between recent gatifloxacin use and hospital treatment for hypoglycemia or hyperglycemia. Similar analyses were also performed on levofloxacin, moxifloxacin, ciprofloxacin, and the second-generation cephalosporins as a group. The macrolide antibiotics were used as the reference group, as this antibiotic class does not directly influence glycemic control.

Main results. Between April 2002 and March 2004, 788 patients were hospitalized for hypoglycemia and 470 patients were hospitalized for hyperglycemia within 30 days after outpatient antibiotic therapy. Compared with macrolide antibiotics, gatifloxacin was associated with an increased risk of hypoglycemia (adjusted odds ratio [OR], 4.3 [95% confidence interval [CI], 2.9–6.3]). A slightly increased risk of hypoglycemia was also seen with levofloxacin (adjusted OR, 1.5 [95% CI, 1.2–2.0]). There was no association noted between hypoglycemia and prior treatment with moxifloxacin, ciprofloxacin, or cephalosporins. As compared with macrolides, gatifloxacin was also associated with an increased risk of hyperglycemia (adjusted OR, 16.7 [95% CI, 10.4–26.8]). There

was no association noted between hyperglycemia and prior treatment with the other antibiotics.

Conclusion. Compared with other broad-spectrum oral antibiotics, gatifloxacin is associated with an increased risk of hypoglycemia and hyperglycemia requiring hospitalization.

Commentary

Gatifloxacin, a fluoroquinolone, is a widely used antibiotic. Fluoroquinolones have become the most prescribed antibiotics in the United States, with 22 million prescriptions written annually [1]. The earlier fluoroquinolones were associated with serious adverse events, such as hepatotoxicity and renal failure, leading to withdrawal of these agents from the market [2]. Because gatifloxacin promotes insulin release from pancreatic islet cells, it may be associated with an increased risk for hypoglycemia. Conversely, gatifloxacin may also increase the risk of hyperglycemia by initiating vacuolation of pancreatic beta cells (thereby reducing insulin levels). However, evidence for these effects has been conflicting and is based on case reports or small studies. Park-Wyllie et al compared risk for hypoglycemia or hyperglycemia in patients treated with various antibiotics and found a strong association between gatifloxacin use and hospitalization for treatment of both conditions. The presence or absence of diabetes in case patients did not affect risk for hypoglycemia or hyperglycemia.

The study's limitations include the inability to evaluate if there was a dose-response relationship between the drug dose and the degree of hypoglycemia or hyperglycemia. The authors also relied on hospital records reflecting ICD-10 codes for hypoglycemia and hyperglycemia to identify case patients. Individuals in the cohort population with dysglycemia may not have presented to the hospital; therefore, the true occurrence of dysglycemia may have been underestimated. However, this potential understimation is true for all antibiotics studied, not just specific to the fluoroquinolones. Finally, these findings are limited to older patients, who may be at particularly high risk for dysglycemia.

Applications for Clinical Practice

Patients older than 66 years, regardless of diabetes status, are

at significantly increased risk for hospitalization for dysglycemia within 30 days of treatment with gatifloxacin. Clinicians should exercise caution when prescribing gatifloxacin to older patients with or without diabetes.

—Review by *Christianne L. Roumie, MD, MPH*

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References

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2. Frothingham R. Quinolone safety and efficacy more important than potency. *Emerg Infect Dis* 2004;10:156–7.