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Warfarin, Sulfonylurea Combo Ups Severe Hypoglycemia Risk

Miriam E Tucker | December 21, 2015

Concurrent use of warfarin and the diabetes drugs glipizide and glimepiride appears to dramatically elevate the risk for severe hypoglycemia in older adults, a new analysis shows.

The findings, from a retrospective Medicare database analysis of adults aged 65 and older, were published December 7, 2015 in the *BMJ* by John A Romley, PhD, associate professor at the Leonard D Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, and colleagues.

The results suggest a "substantial positive association" between concurrent use of warfarin and glipizide or glimepiride and emergency-department visits and hospital admission for hypoglycemia and for fall-related fractures, particularly around the time that patients who are already on the sulfonylurea initiate warfarin.

Beyond just an association — which might be due to patient characteristics correlated with both warfarin use and hypoglycemia risk — the data actually point to the possibility of a significant drug interaction between the medications. "This potential interaction has not been widely appreciated, and healthcare professionals are not routinely alerted when patients on sulfonylureas start treatment with warfarin," Dr Romley and colleagues write.

Close monitoring and patient education are essential for patients who require both medications, principal investigator Anne L Peters, MD, University of Southern California (USC) professor of medicine and director of the USC Westside Center for Diabetes, told *Medscape Medical News*.

"It's a time to readdress the risk for [hypoglycemia] with sulfonylureas, tell patients how to prevent and prepare for lows, discuss the need to eat meals consistently, and reduce the dose of sulfonylurea if the patient is having lows. Preparation of the patient is key," Dr Peters said.

Asked to comment, Kasia J Lipska, MD, an endocrinologist at Yale University (New Haven, CT) who has studied hypoglycemia in the elderly, told *Medscape Medical News*, "I think this is an important study....These are commonly used drugs and they frequently lead to problems that require a hospital visit. This means that we have to pay attention to them and figure out how to make prescribing safer."

Evidence of Drug-Drug Interaction

The study population was derived from a random sample of over 12 million Medicare fee-for-service beneficiaries aged 65 or older from 2006 to 2011. Of those, 465,918 had type 2 diabetes and filled at least one prescription for either glipizide or glimepiride. And among those, 71,533 (15.4%) also filled a prescription for warfarin at some point during the study period.

The primary outcome was emergency-department treatment or hospital admission for hypoglycemia in a given calendar quarter ("person-quarter"). Concurrent use of warfarin and glipizide or glimepiride occurred in 9.6% of all person-quarters.

Overall, emergency-department visits and hospital admissions occurred in 0.018% of person-quarters when warfarin was used in addition to the sulfonylurea vs 0.009% of person-quarters without warfarin use.

After adjustment for age, sex, race, and 14 chronic comorbidities, emergency-department visit or hospital admission for hypoglycemia was significantly more likely during the person-quarters with concurrent use of both medications, with odds ratio (OR) 1.22. The individual rate of hospital admission for hypoglycemia was also significantly elevated (OR, 1.45), while the individual risk for emergency-department visit trended toward significance (OR, 1.17).