DEMENTIA

Cholinesterase inhibitor use link with syncope

Cholinesterase inhibitors, which are commonly prescribed to treat individuals with Alzheimer disease and related dementias, could provoke adverse cardiovascular effects that have serious consequences, a new study reports. "Our findings confirm previous literature demonstrating a link between use of these drugs and development of bradycardia and syncope [fainting]," says lead researcher Sudeep Gill of the Queen's University, Ontario, Canada.

Physicians have debated the benefits of cholinesterase inhibitors, prescription of which is progressively rising in many countries; however, less attention has been paid to their adverse effects. "Although it was known that these drugs could provoke bradycardia and syncope, the magnitude of the risk was unclear and many clinicians were unaware of these problems," Gill comments. "Thus, we also wanted to investigate the potential downstream consequences of this lack of recognition," he adds. Such consequences could include placing a permanent pacemaker in patients presenting with these symptoms, rather than stopping treatment with cholinesterase inhibitors, which might be a more appropriate approach. In addition, elderly people with dementia who have syncope are at high risk of fall-related injuries such as hip fractures.

Gill and colleagues investigated the link between cholinesterase inhibitor use and syncope-related outcomes in a Canadian cohort. The cohort consisted 19,803 adults (mean age 80.4 years) with dementia who were prescribed cholinesterase inhibitors and 61,499 age-matched adults with dementia who were not prescribed cholinesterase inhibitors (controls). Gill's team followed these two groups to see which ones experienced hospital visits for bradycardia, syncope, permanent pacemaker insertion, or hip fracture.

People receiving cholinesterase inhibitors made more hospital visits than did controls. Moreover, compared with the controls, the cholinesterase inhibitor-treated group had a higher frequency of syncope-related outcomes. "We found that use of a cholinesterase inhibitor drug was significantly associated with syncope, bradycardia, permanent pacemaker insertion, and hip fracture," Gill remarks.

These findings have a number of implications. Insertion of pacemakers is costly and holds serious risks of procedure-related complications, as well as being unnecessary for some patients. Furthermore, older patients with dementia experience poor outcomes following hip fracture (resulting from falls during syncope). "The recognition of these serious adverse effects may affect how patients, their caregivers and their physicians view the benefit and risk profile for these drugs," Gill suggests. The researchers implore that the previously under-recognized, serious adverse events highlighted in this study should be carefully weighed against the modest benefits of cholinesterase inhibitors. "In addition, policy makers may be interested in these results because they have important implications regarding the cost effectiveness of these drugs," Gill concludes.

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Original article Gill, S. S. *et al.* Syncope and its consequences in patients with dementia receiving cholinesterase inhibitors. *Arch. Intern. Med.* **169**, 867–873 (2009).