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Adverse Events in Patients Receiving Cholinesterase Inhibitors Due to Dissimilar Follow-up Periods

The study by Gill et al suggested a higher risk of adverse outcomes including syncope, bradycardia, pacemaker insertions, and hip fractures in community-dwelling adults with dementia receiving cholinesterase inhibitors compared with well-matched controls. These findings have important implications, as the agents in question remain the mainstay of symptomatic treatment for an otherwise debilitating illness.

It is interesting to note that while the incidence of hospital visits for syncope are comparatively higher in the cholinesterase inhibitor cohort (2.2% vs 1.5% in controls, see Table 3 in Gill et al), the incidences for all other adverse outcomes are actually almost identical between cholinesterase inhibitor and control groups (hospital visits for bradycardia, 0.5% vs 0.4%; pacemaker insertions, 0.3% vs 0.3%; and hospitalizations for hip fractures, 1.6% vs 1.6%). The significant difference noted in the event rates and subsequent hazard ratios are therefore mainly influenced by the shorter follow-up periods reported for the cholinesterase inhibitor group (hospitalization due to hip fractures, mean follow-up times were 252 days and 302 days for the cholinesterase inhibitor and control cohorts, respectively.) Unfortunately, there was no clarification for this disparity in the article text.

Based on the authors’ description of their method in determining follow-up duration, one could offer the following possible explanations for the discrepancy: (1) subjects in the cholinesterase inhibitor group experienced adverse events much earlier compared with controls, thereby shortening their follow-up time; (2) there was a high rate of drug discontinuation in the cholinesterase inhibitor cohort, resulting in a high number of dropouts from the study; and (3) mortality rate was higher in the cholinesterase inhibitor group compared with controls, resulting in the observed disparity. Any of these scenarios would have important clinical implications that should be explored further.

Previous reviews have identified the clinical benefits of treatment with cholinesterase inhibitors for patients with dementia, especially in patients with Alzheimer disease. However, as highlighted in the study by Gill et al, the possibility of significant adverse events cannot be ignored. Physicians considering their use in frail elderly patients with dementia should be clearly aware of their treatment goal (the preservation of cognitive function) and the need for follow-up monitoring to ensure drug safety.
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HEALTH CARE REFORM

Are We Providers or Physicians?

I read with interest the comments made in a recent issue concerning pharmaceutical sales.¹ Undue pressure masked as marketing is inappropriate, but physicians must make decisions concerning new agents based on information given to them by pharmaceutical companies, since the initial studies of new agents are sponsored and paid for by the pharmaceutical companies. When pharmaceutical representatives come into my office with their information, studies, and samples, I am aware that they are sponsored by their company. This is akin to watching a commercial for the product.

In my outpatient practice, the lunches I eat, and will continue to eat as long as it is legal, help me and my office staff with our expenses as well as help us to learn valuable information concerning new products. The samples I receive are invaluable to my patients.

One of my close personal friends runs a business where he sells lunches to the drug companies for their distribution. In my discussions with him, if additional cuts are made in this area, many small catering businesses will go out of business. The money spent by the drug companies does not evaporate but circulates through our economy.

However, direct-to-consumer marketing of prescription drugs is inappropriate, and often advertisements are downright silly and even condescending. These ads market drugs to persons who cannot write prescriptions. They must be effective, because each year more millions are spent on these ads while pressure is being placed on these companies to eliminate marketing to physicians, who make clinical decisions and actually write prescriptions. It is also interesting to me that the national media has been relatively silent about these print and media ads. Prime-time television is filled with pharmaceutical ads for prescription medications. Could this be influencing the lack of outcry spent on this aspect of the pharmaceutical business?

The pharmaceutical companies are not the enemy. Without free-market forces operating within this industry, new drug development will be diminished, resulting in the decrement in the quality and quantity of medicines and therapies. Americans have come to expect the constant development of new therapies. If the government tries to externally micromanage the pharmaceutical industry drug development will be greatly limited. The health of all of us is at stake.

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