Underreporting of Hemorrhagic Stroke Associated With Phenylpropanolamine

To the Editor: Although passive surveillance systems for adverse drug event reporting are often used to detect rare, serious adverse reactions for marketed drugs, they are limited by underreporting. The extent of underreporting is unknown and may be influenced by the severity of the event, the specialty of the reporter, how long the drug has been on the market, whether the event is labeled, and whether the drug is prescription or nonprescription. We attempted to assess the degree of underreporting of hemorrhagic stroke associated with phenylpropanolamine, a nonprescription drug.

Methods. We compared the number of cases of hemorrhagic stroke associated with phenylpropanolamine detected in the Hemorrhagic Stroke Project with those reported during the same period to the Adverse Event Reporting System of the US Food and Drug Administration (FDA). The Hemorrhagic Stroke Project study was conducted between December 1994 and July 1999 in Connecticut, Massachusetts, Ohio, Kentucky, Rhode Island, and Texas. In an effort to recruit all research subjects who were 18 to 49 years of age and in the target age group, 27 of whom had been exposed to phenylpropanolamine. During the same period, no states or hospitals in the study area reported cases to the Adverse Event Reporting System. The reporting rate was thus 0% (95% confidence interval, 0%-10.5%).

Comment. This very low rate of passive reporting is consistent with previous estimates. Scott et al estimated that less than 1% of suspected serious adverse reactions were reported to the FDA in the 1980s. Rogers et al found that physicians reported only 8% to 13% of serious or life-threatening adverse reactions. We were unable to identify any prior studies of underreporting of a serious adverse reaction caused by a nonprescription drug in the United States.

Lois La Grenade, MD, MPH
David J. Graham, MD, MPH
Parivash Nourjah, PhD
US Food and Drug Administration
Rockville, Md