Epilepsy Community Has Major Concern Over Release of Anticonvulsant Drug Comparison Report

Landover MD, February 16 -- Leading representatives of the Epilepsy Foundation, American Epilepsy Society, American Academy of Neurology, Finding A Cure for Epilepsy and Seizures, National Association of Epilepsy Centers, and the North American Regional Commission of the International League Against Epilepsy today reported they have grave concerns about the implications and potential misuse of the anticonvulsant (AED) drug comparisons study recently released by the U.S. Agency for Health Research and Quality (AHRQ). The study’s intent is to provide an evidence-based analysis of the Effectiveness and Safety of Antiepileptic Medications in Patients With Epilepsy. But the AHRQ report has little clinical value according to the specialists in neurology and epilepsy and could negatively impact patient care.

The AHRQ report is an examination of the comparative efficacy, safety, and tolerability of newer versus older and innovator versus generic antiepileptic medications. The representatives and their organizations strongly support evidence–based medicine and comparative effectiveness research, which they believe improves quality of care. At issue, however, is the study focus, which fails to recognize the different types of epilepsy and deals with this multiform disorder as if it were a monolithic and homogeneous condition. The study further compares effectiveness of old-line anticonvulsants to newer epilepsy drugs irrespective of epilepsy type. Given that seizures have vastly different pathologies and the use of AEDs differs greatly based on the underlying pathology, the old versus new comparison is irrelevant to clinical practice.

Brien Smith, M.D., Chair of the Epilepsy Foundation Board of Directors states, “The Epilepsy Foundation has strong concerns with this report being used to advise patients, clinicians, and/or insurers. It was also greatly disappointing that the most prominent organizations serving people with epilepsy, and the professional organizations that pave the way for increased quality in epilepsy research and care, had such a minimal or nonexistent impact on a report from the Effective Health Care Program – including myself as a key informant on the research project.”

Dr. Smith continues, “We continue to believe that this report will create a negative impact on the care of patients or that the research will be irrelevant to practice.”

Tony Coelho, President & CEO of the Epilepsy Foundation says, “This is incredibly disappointing not only as an example of stakeholder input and review, but also of the importance of the Effective Healthcare Program overall. We join our partner organization in expressing hope that this is not a template or model for patient and physician engagement on CER research projects.”

“The major problem is the shoehorning of all new drugs and most old drugs into two groups,” notes Edward Faught, M.D., of Emory University, and who chairs the American Epilepsy Society’s Treatments Committee. “The study author’s assertion that differences between the groups are not too marked to allow pooling defies biological credibility and may lead to dangerous decisions based on economic factors alone.”
The AHRQ report concludes there are, “No significant differences in the risk of maintaining seizure freedom” when newer antiepileptic medications were compared versus carbamazepine (CBZ), phenytoin (PHT), and valproate (VPA).

“It is possible to read the conclusions simplistically and to determine that there is little justification for not using carbamazepine or valproate first,” Faught says. He notes also that the study’s equivalent efficacy results between old and new drugs depend heavily upon the inclusion of two drugs in the analysis that are less effective for new-onset seizures, gabapentin and vigabatrin. The first is known to be relatively inefficacious for these seizures, while the latter is a rarely used special-purpose anticonvulsant.

Medication side effects and potential drug-drug interactions also are given relatively little attention in the study. Valproate has a well-documented increased risk of hypatotoxicity in children under two years of age, and an increased risk of dermatological reactions in children. Particularly disconcerting to the specialists is the absence of consideration of the teratogenic effect of this drug, which should be avoided when possible due to the risk of serious congenital malformations and cognitive outcome in children of women taking the drug during pregnancy. Particular side effects associated with carbamazepine and phenytoin can also make these medications inappropriate for certain types of patients.

Those troubled by the comparative report on anticonvulsants acknowledge that it is of necessity an analysis of relevant research that has been conducted to date. But too few studies on all types of epilepsy are available to provide useful answers in regard to the comparative efficacy, safety, and tolerability of newer versus older and innovator versus generic antiepileptic medications.

Michael Privitera, M.D., of the University of Cincinnati, observes that, “The study includes objectives that do not reflect important nuances in the treatment of epilepsy. For example,” he says, “there does not seem to be a distinction between new onset and refractory seizures. In addition, the issues about efficacy and effectiveness of antiepileptic drugs and medication substitution should be considered separately.”

Privitera notes further that, “The technique of meta-analysis has many pitfalls and all researchers agree that randomized prospective trials specifically addressing the question of how the old antiepileptic drugs compare to the newer ones are desperately needed.” Evidence presented in the AHRQ study is described in the report itself as either “insufficient,” “of low strength,” or “not very informative.” The specialty organizations agree. Because of these limitations and other problems they believe are in the study design and development, the patient and professional organizations are urging the AHRQ to withdraw its anticonvulsants report, and to collaborate with their organizations to define a more appropriate research proposal.

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