



erc
epilepsy RESOURCE CONNECTION

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hotline

Mandatory Generic Substitution of Antiepileptic Drugs Raises Concerns

Mandatory generic substitution of antiepileptic drugs (AEDs) is raising concerns among physicians and patients that this increasingly common practice is causing a rise in breakthrough seizures and subsequent adverse effects, 2 new studies suggest.

Presented at the First North American Regional Epilepsy Congress, the first study compared switchback rates from generic to brand-name AEDs (*Lamictal*, *Frisium*, *Depakene*) and compared them with drugs for other chronic conditions, including high cholesterol and depression (*Zocor*, *Prozac*).

Switching a patient from a branded cholesterol medication to a generic agent is unlikely to have significant consequences for the patient in the short term. In comparison, the consequence of a breakthrough seizure can be devastating and life altering. A seizure in someone who is seizure-free can have a profound impact. It can have many consequences, including injury, driving restrictions, and embarrassment. . .

Investigators at the Montreal Neurological Institute, in Quebec, found the switchback rate from generic AEDs was 12% to 19%, compared with just 2% to 3% in drugs for depression or high cholesterol.

"These were very striking results, and I think it would be worthwhile to conduct further research to explore the reasons this is occurring from both clinicians' and patients' perspectives," said principal investigator Frederick Andermann, MD, from the Montreal Neurological Institute.

Using a public payer database from Ontario of pharmacy claims from January 2002 to March 2006, researchers found a total of 1452 patients on *Lamictal* — 437 on monotherapy and 1015 on polytherapy — were converted to the generic version of the drug.

Of these, 12.9% switched back to the branded medication. Switchback rates for the other 2 AEDs were about 20% — both of which were significantly greater than switchback rates for *Zocor* (1.5%) or *Prozac* (2.9%). In addition, patients who were taking branded *Lamictal* increased their average daily dose from 229.5 mg at baseline to 279 mg with the generic agent.

The second study, a national survey led by Michel Berg, MD, from the University of Rochester, NY School of Medicine, explored US physicians' and patients' attitudes toward generic AED substitution. It included 550 adult patients diagnosed with epilepsy and 606 physicians treating epilepsy, who completed an online survey. 75% of physicians and 65% of patients reported concern over the safety of generic medications. Furthermore, 90% of physicians reported a specific concern that generic substitution in controlled patients could result in a breakthrough seizure.

In addition, 65% of physicians reported they had cared for a patient who had experienced a breakthrough seizure caused by a switch from a branded to a generic agent.

Both Drs. Andermann and Berg say there is a significant and long-standing belief and concern among clinicians that generic AED preparations don't offer the same therapeutic effect as branded medications.

The general assumption is that the wider range of bio-available levels in generic agents compared with the branded drugs causes breakthrough seizures to happen. [CONTINUED ON BACK]

Treating Sleep Apnea May Reduce Seizure Frequency

Treating obstructive sleep apnea (OSA) may significantly reduce seizure frequency in patients with refractory epilepsy, a new pilot study suggests.

The trial showed that approximately one third of subjects who received continuous positive airway pressure (CPAP) treatment had a 50% or greater reduction in seizure frequency, compared with 15% of subjects who improved on placebo.

"These results are very promising and very exciting, because even though our study wasn't powered to find a statistically significant effect, we did observe a significant trend toward improvement in seizure frequency among patients who received CPAP — a result that rivals that of an antiepileptic drug," said principal investigator Beth Ann Malow, MD, from Vanderbilt University, in Nashville, Tennessee.

Funded by the NINDS, the study included 35 adult patients ages 21-60 with refractory epilepsy who had a minimum of 2 seizures per month and who also had a diagnosis of OSA.

A growing recognition among the scientific community of a definite link between OSA and epilepsy led to the study.

One possible explanation for poor-quality sleep in individuals with epilepsy may be the tendency to have sedentary lifestyles and daytime sleepiness, effects that are frequently attributed to the sedating effects of antiepileptic drugs (AEDs).

Whatever the reason, research suggests that poor-quality sleep can lead to increased seizures. While the mechanism is not entirely clear, the current thinking is that sleep deprivation increases neuronal excitability, which in turn triggers and increases seizure frequency.

In the general population sleep apnea occurs in 1 in 4 men and 1 in 9 women. Among individuals with epilepsy, however, Dr. Malow said preliminary evidence suggests the incidence could be as high as 40%.

While larger studies are needed to confirm the incidence, Dr. Malow noted that this still amounts to a significant number of individuals who could potentially benefit from treatment of OSA.

"Treating sleep apnea could provide clinicians with a novel way to try to treat seizure frequency in a significant proportion of epilepsy patients. If these results bear this out it could offer clinicians another treatment option."

Malow's team is currently designing a much larger, multicenter trial to see if the results of the pilot study can be confirmed.

In addition to a reduction in seizure frequency, Malow is interested in looking at other potential benefits of treating OSA in patients who have good seizure control. "We don't necessarily want to limit our study to the refractory-epilepsy population, and seizure frequency isn't necessarily the only end point we want to look at. It could be that patients who are seizure-free may also benefit from CPAP treatment. For instance, if we can improve the quality of their sleep, this may result in less daytime sleepiness, needing fewer medications, and improvement in quality of life, which may be just as important as seizure control." ❖ M E D S C A P E (First North American Regional Epilepsy Congress)

GENERIC DRUG SUBSTITUTION [continued from front]



Dr. Berg agreed, pointing out that despite the fact that his study shows 65% of physicians have cared for patients with breakthrough seizures as a result of switching from a branded to a generic agent, this finding is not reflected either in the scientific literature or MedWatch, the FDA's safety information and adverse event reporting program.

According to Dr. Berg, "The word on the street is that this problem is much bigger than the literature suggests in that physicians are not using the voluntary reporting system put in place to detect these adverse drug events, and clearly the results of our study bear this out." Their results should be a call to physicians who treat people with epilepsy to report any events related to generic substitution. This is becoming increasingly important because many more generic AEDs are expected to come on the market within the next few years.

In the meantime, the issue has generated sufficient concern within the neurological community that several organizations, including the American Epilepsy Society (AES), the Epilepsy Foundation of America, and the International League Against Epilepsy, have all established working groups to generate position papers on generic substitution of AEDs. Dr. Berg heads the AES working group.



While switching a patient from a branded cholesterol medication to a generic agent could cause an increase cholesterol levels, it is unlikely to have significant consequences for the patient in the short term. Such a scenario, he said, would likely be managed by simply adjusting the dose of the generic agent.

In comparison, the consequence of a breakthrough seizure can be devastating and life altering. A seizure in someone who is seizure-free can have a profound impact. It can have many consequences, including injury, driving restrictions, and embarrassment, among many others.

In addition, Dr. Berg's study also showed that 62% of patients and 75% of physicians were aware that pharmacists have the authority to substitute a branded AED for a generic without physician consent. However, only 43% of physicians were aware of mandatory generic substitution laws for branded prescription medications.

Dr. Andermann noted that, in Ontario, patients who do not want generic substitution of their AEDs must seek special permission; otherwise the pharmacist is bound to dispense a generic substitute.

Dr. Berg's study also showed that 81% of patients and 87% of physicians believe pharmacists should be able to substitute a brand name AED with a generic only with physician consent.

While Dr. Berg acknowledged the importance of containing health-care costs, he added that cheaper medications are not the only costs that should be included in the equation.

When considering generic substitution, we also have to include the potential cost of lost efficacy and increased side effects.

✦ MEDSCAPE (First North American Regional Epilepsy Congress)

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Winter fun & games

Sat. Feb 3, 2007

10:00 a.m. - 1:30 p.m.

@ ERC (2919 W. 2nd Street)

Fun, lunch and connect with other families facing similar challenges of living with a seizure disorder. Includes free lunch (donations are accepted to help defray costs.)

Pull the kids away from the cartoons... And join other families affected by epilepsy for a morning of indoor fun for all ages! We will have inflatables for the kids to bounce in.

Adults will enjoy a challenging game of Cronium! If you haven't played it, imagine combining charades and a trivia game. Everyone can contribute giving their team a moment to shine.

To attend, please RSVP at (316) 943 - 2453

Lifespan Respite Care Act Passed

On December 21, 2006, the Lifespan Respite Care Act (H.R. 3248) was signed into law. Rep. Michael Ferguson (R-NJ) lead the sponsorship in the House. On December 6, 2006, the House of Representatives passed H.R. 3248, sponsored by Reps. Ferguson and Jim Langevin (D-RI).

On December 8, 2006, the bill was approved by voice vote in the Senate. Senators Hillary Clinton (D-NY) and John Warner (R-VA) co-sponsored the Senate version. The original majority co-sponsor, Senator Olympia Snowe (R-ME), has also remained a champion on the bill, and ultimately helped secure final Senate passage.

The final version of the Lifespan Respite Care Act provides \$30 million in the first year and almost \$300 million over 5 years for competitive grants for states and local agencies to increase the availability of respite care services for family caregivers of individuals with special health care needs regardless of age. Family caregivers provide 80% of all long term care in the United States. The unpaid care is valued at more than \$300 billion a year. ☺EF

Adult Epilepsy Support Group

Meets Second Tuesday of Month, 6:30 PM • 2919 W. 2nd Street, Wichita

Jan. 9th: "Resolved: Less Seizures in 2007"

Feb. 13th: "Epilepsy in the Work Place"

VNS Therapy® Presentation

Cyberonics and Via Christi Comprehensive Epilepsy Center host a monthly luncheon presentation on VNS THERAPY® for patients and their families. The session includes time for questions & answers. For more information or to make a reservation to attend, call: 316/617-9795



You must RSVP to attend.

11:30 a.m. - 12:30 p.m.

Third Wednesday of the month
(Jan. 21st; Feb. 20th)

